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BULLETIN of the JOHNS HOPKINS HOSPITAL

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January, 1952

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INTRODUCTION TO SERIES OF PAPERS ON CHRONIC CONSTRICTIVE PERICARDITIS

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Received for publication November 1, 1951

The historical landmarks in the development of the diagnosis, the physiopathology and the treatment of chronic constrictive pericarditis are of interest but will not be considered in detail here. Dr. Paul White gave an excellent account of these in the St. Cyres Lecture in 1935. It may not be amiss to mention the descriptions of this condition by Lower (1669), Lancisi (1728), Cheever (1842), Wilks (1870), and Pick (1896); the advocacy of decortication by Delorme (1898); the successful operations by Rehn (1913), Sauerbruch (1913), Schmieden (1918), and Churchill (1928); the classical paper on diagnosis by Volhard (1923); the experimental production of the condition by Beck and Griswold (1930); and the clinical physiological studies by Burwell and associates (1932).

Among the current problems of interest is the time at which decortication should be performed. It is fairly generally agreed that the tubercle bacillus is the most frequent causative agent, and Churchill and others have commented upon the dangers and difficulties of operating in the presence of an active infection. The introduction of antibiotic agents such as streptomycin and para-aminosalicylate may have altered the situation. Holman and Willett have recently reported favorable results in the treatment of active tuberculous pericarditis by the combination of streptomycin therapy and pericardiectomy. A larger experience and a more prolonged follow-up period are required before an accurate assessment of this therapy can be made. Since "inflow stasis" occurs not infrequently in tuberculous pericarditis with effusion and since many cases do not progress to chronic constrictive pericarditis, obvious difficulties in the selection of cases for early pericardiectomy are present.

Much has been written about the site of decortication and the choice of incisions. It is fairly generally agreed that it is constriction of the right side of the heart and its entering veins which in most cases is responsible for the major part of the disability. The recent report by White et al. demonstrates quite clearly that in some cases constriction of the left side of the heart causes the major part of the difficulty. The logical conclusion would appear to be that both the right and left sides of the heart should be decorticated. After having used first a left parasternal incision with inadequate exposure and next a median sternotomy with improved but still somewhat inadequate exposure, I prefer a left anterolateral transpleural incision in the fourth interspace with

division of the fourth and fifth costal cartilages. Both the right and left sides of the heart can be approached through this incision. It does not matter greatly if the right pleural cavity is entered provided the injury is recognized and pulmonary inflation is maintained.

The following papers in this issue of the Bulletin do not represent a cooperative study but are rather the results of independent investigations. Although the diagnosis of chronic constrictive pericarditis is not usually difficult to arrive at on clinical grounds with the aid of usually readily available laboratory technics, as pointed out in the first paper by Dr. McKusick, help and corroboration are afforded by the methods discussed in the subsequent papers by McKusick on electrokymography and roentgenography, and by Scarborough et al. on ballistocardiography. More important than the diagnostic potentialities of these methods is the light that they shed on the pathological physiology of chronic constrictive pericarditis. Furthermore, these observations aid in the understanding of normal cardiac function and the disturbed circulatory dynamics in other forms of heart disease.

Dr. Davis and Dr. Isaacs approach the study of constrictive pericarditis by means of experimentally produced cardiac constriction. Davis' interest is primarily in the changes in renal hemodynamics which occur in this form of congestive heart failure and in the associated salt and water retention. In a subsequent issue of the Bulletin Isaacs' work on the cardiac and pulmonary hemodynamics, with special reference to the pathological physiology of localized constriction of the right or left side of the heart, will be published. The importance of decorticating both the right and the left ventricles is demonstrated.

This group of papers should be of value to those interested in the clinical and experimental aspects of heart disease.

CHRONIC CONSTRICTIVE PERICARDITIS

I. Some Clinical and Laboratory Observations

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Received for publication August 13, 1951

The cases which are described here in some detail constituted the patient material for an electrokymographic and roentgenkymographic study which is reported in an accompanying paper. Clinical features, angiocardiograms, cardiac catheterization data, renal clearance determinations, and results of pericardectomy are of considerable interest and are presented in this report.

Case 1. S. W. A. In 1923 this white male patient, born in 1897, had, for several months, chest pains so severe he "had to take 18 aspirins a day". A positive serologic test for syphilis was found and treatment instituted. He was well until 1945 when there was onset of symptoms consisting of fever, chills, weakness, and progressive abdominal swelling. He was a confirmed alcoholic. For two years he was believed to have Laennec's cirrhosis. Several "peritoneal button" operations were performed with limited benefit. At the time he was studied in 1948 shortness of breath, ascites and leg edema were the main manifestations. He had been unable to work since the onset of his illness three years previously. The main features of the physical examination were limited thoracic expansion, greatly distended veins of the neck and arms, liver enlargement to a point 5 inches below the right costal margin, and slight cardiac enlargement. The blood pressure was consistently about 110/80 mm. Hg and there was a slight but definite pulsus paradoxus. X-rays revealed a dilated superior vena cava, slight cardiac enlargement and no pericardial calcification. The arm venous pressure was 320 mm. of saline with no significant change after digitalization. The arm-to-tongue circulation time (Decholin) was 18 seconds. Operation was performed on November 4, 1948, by Dr. Alfred Blalock. Through a median sternotomy incision the entire anterior surface of the heart was exposed. There was dense fibrosis in the groove between the right ventricle and right auricle and this fibrous process encircled the right auricle and both venae cavae in an extensive manner. There was almost no involvement of the ventricles themselves. Over the right ventricle the pericardium was thickened but there was no evidence of involvement of the epicardium in this area. The pericardium bound to the right auricle and venae cavae and a large portion of the pericardium overlying the right and left ventricles were successfully removed. Post-operatively the venous pressure fell to normal in the first week, the liver shrank to a position just below the costal margin, and there was no further evidence of fluid accumulation. Five months following operation the patient returned to a full work program. He has remained well almost three years following operation and works as a merchant seaman.

Case 2. R. McA. This is a white male patient born in 1922. In 1942 the patient developed transient episodes of nausea, vomiting, weakness and easy fatigability. These episodes continued for about two years. In 1945 he was rejected by the service because of "organic heart disease". The patient was able to do unusually heavy labor without difficulty until 1948

when after a period of exertion he became nauseated, "weak in the knees", and lost consciousness. His physician told him his heart "beat a little too fast" and prescribed digitalis. In the next few months the patient began to feel progressively less well and there was weight gain with abdominal swelling. Significant physical findings preoperatively in 1949 were moderate generalized venous distension (venous pressure 270 mm. saline), enlargement of the heart to the left and right, auricular fibrillation, split and accentuated second pulmonic sound, split first sound at the apex, liver down three cm., bilateral varicoceles, and blood pressure 100/70. Digitalization had no effect on the elevated venous pressure. X-rays revealed very extensive calcification of the pericardium. On February 16, 1949, pericardectomy was performed by Dr. Alfred Blalock using a median sternotomy incision. To the left the decortication was extended far around onto the left ventricle and on the right as far as the venae cavae; inferiorly the diaphragmatic surface was freed as far as the central tendon. Only a plaque of calcium in the region of the left anterior descending artery was left. When restudied in April 1949, venous pressure was 75 mm. in the right arm, 135 mm. in the left; the liver was down 2 cm. and there was no fluid accumulation. In June 1950 auricular fibrillation had reappeared. However, the liver was not palpable, heart sounds were normal, and there had been no edema or unusual dyspnea. The patient had been doing heavy labor. Venous pressure was 80 mm. saline. In May, 1951, the findings were the same. He had been maintained on digitalis during the previous year and had not missed a single day from his work with a construction crew.

Case 3. A. N. This is a white male patient born in 1897. His pertinent history begins in 1920 at which time he developed shortness of breath and abdominal swelling, was hospitalized for 9 months and told he had "water on the heart". He recovered from that illness, however, without significant physical disability. In 1936 "overnight" he began to have abdominal swelling, leg edema and dyspnea. In 1944 a partial pericardectomy was performed at a New Orleans hospital using a left precordial incision. The decortication was considerably limited by serious bleeding, probably due to a small rupture of the left ventricle. Thereafter, however, he had almost complete relief of symptoms and no longer required frequent abdominal paracenteses as before. In 1946 again "overnight" his previous symptomatology returned. With this he complained of severe precordial pain for which opiates were given to the point of addiction. These were his complaints when studied in 1949. The positive physical findings were greatly distended neck and arm veins, limited chest expansion, enlargement of the heart to a point 2 cm. beyond the left midclavicular line, blood pressure 108/80 with slight but definite pulsus paradoxus, a protodiastolic sound, liver down 5 finger-breadths. In the left mid-precordium at the site of the rib defect, the cardiac impulse was quite forceful. There was an outward movement with ventricular filling which was quick and slapping, making it possible to suspect the "flat-top and V's" EKY pattern described elsewhere (2). X-ray of the chest revealed extensive pericardial calcification, particularly on the diaphragmatic surface, cardiac enlargement, a dilated superior vena cava, and extensive pleural thickening bilaterally. Fluoroscopy revealed reduced pulsations everywhere except for an area at the cardiac apex which appeared almost herniated and which had a gross "flat-top and V" type of movement. Venous pressure was 275 mm. saline, vital capacity (3 sec.) 1.0 liter, arm-to-tongue circulation time 40 sec., arm-to-lung circulation time 26 sec. On September 7, 1949 pericardectomy was performed by Dr. J. L. Southworth via a median sternotomy. All portions of the heart visualized except for the apex itself were involved in a very dense calcific and fibrotic process. The entire anterior portion of the right ventricle, right auricle and venae cavae was decorticated. Post-operatively the liver receded moderately in size, venous pressure fell to 130 mm. saline, arterial pressure rose to 130/70 and the previously rapid fluid accumulation ceased. Five weeks following operation auricular

flutter appeared and the day following this event the patient developed a right hemiplegia which was believed to be due to embolism from the left auricle. Recovery from this accident was very slow with respect to both speech and the use of arm and leg. It did have one desirable effect: the patient's addiction disappeared completely.

Case 4. L. P. W. In October 1949, this colored male patient born in 1902 had the onset of an acute febrile illness characterized by productive cough and bilateral pleuritic pain. He was studied at a Washington, D. C., hospital and found to have a left pleural effusion and a large pericardial effusion. These slowly cleared and he was able to return to work in February 1950. At about this time, however, he noted swelling of the face in the morning and of the ankles at night. A prominent protodiastolic third heart sound was recorded. Abdominal swelling and exertional dyspnea appeared and he found it necessary to sleep on two pillows. In July 1950, significant findings included B. P. 135/110 with pulsus paradoxus, generalized venous distension, right pleural effusion and ascites, hepatomegaly and hyperbilirubinemia. On July 19, 1950, median sternotomy was performed by Dr. Richard Kieffer who found a dense fibrous scar encasing the entire heart. The heart was rotated clockwise and mainly the right ventricle and a portion of the right auricle were decorticated. The posterior part of the heart—mainly left ventricle—was freed from the overlying pericardium by blunt dissection. Ventricular fibrillation developed during operation but was successfully reverted with cardiac compression and procaine amide (Pronestyl Squibb). Histologically the pericardial scar showed tubercles. Streptomycin, 1 gm. a day, was started five days before operation and continued for a total of two months. Following a stormy post-operative course the patient gradually improved. Venous pressure returned to normal and the liver receded to the costal margin. After nine months of rest he returned to work as a teacher.

Case 5. C. L. M. This white male patient born in 1891 had no history of acute pericarditis or tuberculous disease. There had been rheumatoid arthritis of moderate severity for ten years beginning in 1940. In August 1949, the patient sustained a fracture of two vertebrae as a result of a steam-boiler explosion which threw him several yards. He was rendered unconscious for two hours but recalls no symptoms referable to the heart or lungs. Later in 1949 there was the onset of occasional evening pedal edema. In June 1950, there was the abrupt onset of severe right upper quadrant pain and sensation of fullness of the head when he leaned over or lay flat. The most significant findings in July 1950 were generalized venous distension (venous pressure 270 mm. saline in arms and legs), slight cardiac enlargement, scratchy heart sounds with a protodiastolic sound, hepatomegaly, and a dilated superior vena cava by x-ray. Pericardectomy was performed on July 28, 1950 by Dr. Alfred Blalock using an incision in the fourth left interspace. Overlying the right ventricle and right auricle and between these chambers and the sternum was a large, thick-walled cyst containing 300 cc. of material which resembled dark coffee. The walls of the cyst were parietal and visceral pericardium; the cyst resembled a subdural hygroma. In other areas the pericardium was adherent to the epicardium and was thickened. A wide decortication of both ventricles was performed. Following operation venous pressure fell promptly to normal, the liver decreased in size, fluid accumulation ceased, and all symptoms—particularly the sensation of fullness in the head—disappeared. Post-operatively, coincident with the decrease in liver size, a conspicuous hepatic friction rub was observed over a two week period. The patient has now remained well one year following pericardectomy.

Case 6. L. N. N. This is a white male patient born in 1934. An older brother has had pulmonary tuberculosis. At the age of two or three years the patient had cervical adenitis and fever for several weeks. At the age of 13 he developed a severe productive cough and fever persisting for 10 days. Shortly thereafter a pulmonary lesion was found and interpreted as tuberculosis, although no organisms were identified and the tuberculin skin test was said

to be negative. In 1949 he developed anorexia, nausea, vomiting, easy fatigability, headache and fever. This persisted for one month, gradually subsiding. Three months later abdominal swelling was noted. This progressed to the point that paracenteses were necessary. Ankle edema appeared. When first seen in December 1949, examination revealed low grade fever, tachycardia, generalized venous distension, hepatomegaly, ascites, and ankle edema. Significant laboratory data included alkaline phosphatase 11.5 units per hundred cc., bilirubin 3.6 mgms. per hundred cc., 26% BSP retention in 30 minutes, venous pressure of 260 mm. saline in arms and legs, EKG compatible with chronic pericarditis, positive tuberculin skin test (1:1000 O.T.). Because of persistent fever, pericardectomy was deferred. On a second admission in April, 1950, the blood pressure was 90/60 with definite pulsus paradoxus. The right leaf of the diaphragm was elevated. The sounds were tic-tac in quality and distant. There was a scratchy systolic sound at the apex varying with respiration. Because of continuing fever and the development of a pleural friction rub operation was again considered inadvisable.

On the third admission in July, 1950, it was found that the patient's condition had deteriorated further with rapid accumulation of fluid and depletion of serum proteins to 4.1 grams per hundred cc. Pericardectomy was performed on July 25, 1950 by Dr. Alfred Blalock using an incision in the fourth left interspace. A dense pericardial scar was successfully removed from the largest portion of both ventricles and a part of both auricles. Grossly the left dome of the diaphragm was studded with tubercles and histologically the pericardial scar revealed tubercles. The patient improved with amazing rapidity. Serum proteins rose from 4.1 to 6.1 (albumin from 2.3 to 3.5 gms. per hundred cc.) in two weeks. Venous pressure fell to normal in the first twenty-four hours and remained so. Fluid accumulation ceased. The patient was treated with dihydrostreptomycin and para-amino-salicylic acid for 50 days. The patient is considered a clinical cure.

On Thanksgiving Day, 1950, the patient sustained trauma to the head. This was followed by development of manifestations of tuberculous meningitis for which he has been treated with streptomycin intramuscularly and intrathecally, together with para-amino-salicylic acid intravenously. His course has been satisfactory and it is anticipated that he will recover. This experience indicates the necessity for prolonged anti-tuberculosis therapy in cases such as this with active disease at the time of operation (1).

Case 7. W. B. This white boy, born in 1934, had very acute development of abdominal swelling with no other symptoms one month before first being seen in August, 1950. He had previously been in excellent health and engaged actively in sports particularly baseball. He was exposed to the maternal grandfather and a maternal uncle, both of whom died of tuberculosis. Examination revealed generalized venous distension (venous pressure 330 mm. saline), mulberry cyanosis of hands, feet, lips and ears, blood pressure 110/90 with definite pulsus paradoxus, right pleural effusion and ascites, a calcified placque over the left ventricle, enlarged left auricle and dilated superior vena cava by x-ray, liver down four finger-breadths. In the left mid-precordium there was a visible and palpable impulse with suggestively "flat-top and V" characteristics (2). There was a conspicuous protodiastolic heart sound. Pericardectomy was performed by Dr. Henry Bahnson on September 11, 1950, through an incision in the fourth left interspace. The exposure permitted resection of scar from the venae cavae anteriorly to a point well around posteriorly on the left ventricle. There was no clue as to the etiology of the process. Venous pressure fell to about 140 mm. water following operation, fluid accumulation ceased, and the patient has been asymptomatic for ten months.

Case 8. J. M. This was a colored male patient, born in 1893, who in 1944 had onset of leg edema and dyspnea. This increased slowly but progressively until the time of his admission to the hospital in 1949. Significant physical findings were marked generalized venous

distension, enlargement of the heart to right and left, auricular fibrillation, a superficial crunchy pericardial sound in the left mid-precordium, liver 10 cm. below the right costal margin, bilateral varicoceles, ascites, and 2 plus ankle edema. The blood pressure was 104/90 mm. Hg, the venous pressure 370 mm. saline. X-rays revealed extensive pericardial calcification. The cardiac apex was free of calcification and on fluoroscopy showed a distinct "flat-top and V" type of movement (2) of quite large amplitude. EKG's showed auricular fibrillation and right axis deviation. On January 16, 1950, exploration was performed by Dr. J. L. Southworth via a median sternotomy incision. There was a very extensive calcified shell surrounding all portions of the heart visualized. Decortication was undertaken and when approximately one-half the anterior cardiac surface had been freed the right ventricle which had ballooned up during the procedure ruptured. Attempts to repair the large rent only made it larger, the myocardium being too friable to hold sutures. The patient exsanguinated. Autopsy confirmed the clinical impressions: the left auricle was considerably dilated. There was no definite evidence of tuberculosis.

Case 9. N. D. This white male patient born in 1915 had a sister with pulmonary tuberculosis treated by pneumothorax. At the age of fourteen, there was an illness characterized by sudden prostration, chest pain, and cough following which dyspnea on exertion was noted. At the age of 16 a tentative diagnosis of tuberculosis was made and sanatorium care recommended. At age 18 dyspnea became worse; ankle edema was noted and he was told he had a weak heart. Dyspnea on unusual exertion continued and became gradually worse. Physical examination in May, 1949, revealed moderate venous distension in the neck, heart of normal size, liver down five finger-breadths. Laboratory data included venous pressure varying between 138 and 235 mm. saline, circulation time 23 seconds (Decholin), and a triangular, slightly enlarged heart with calcification of the postero-inferior portion of the pericardium. The general physical condition was the same or slightly improved when studied in detail again in November, 1949, and in February, 1950. On examination in June, 1950, it was found that the patient's only symptom was dyspnea on unusual exertion. The liver was down two finger-breadths but there was no ankle edema. X-rays revealed a dilated superior vena cava, enlargement of the heart to the right, and pleural thickening on the right. Venous pressure was 160 mm. saline. (Operation was decided against because of the patient's relatively slight incapacitation.) His status was identically the same in July, 1951.

Case 10. W. M. This white male patient born in 1893 had onset of easy fatigability late in 1948 and blueness of the lips and nails late in 1949. He was told by a physician that there was calcium around his heart. There was occasional slight ankle edema. He was digitalized without evident benefit. There was one syncopal attack of five minutes duration following descent of a flight of stairs. The patient's health had been excellent prior to the development of the above symptoms. There was no known exposure to tuberculosis. Physical findings included blood pressure 180/100, cyanosis of lips, ears and nailbeds, distention of the neck veins, a prominent protodiastolic sound, liver down three finger-breadths. Laboratory findings included venous pressure 140 mm. saline, normal hemogram (Hgb. 15 gms.), arterial oxygen saturation 87%, heart normal in size by x-ray with extensive calcification overlying both ventricles and 10% methemoglobinemia (the last subsequently disappeared). In an attempt to improve the patient's functional status pericardectomy was attempted on September 18, 1950, by Dr. Alfred Blalock using an incision in the fourth left interspace. From the beginning heart action was seen to be very feeble and cardiac standstill occurred before any decortication could be performed. Autopsy revealed a very extensive *ossified* shell about both ventricles (*Panzerherz*) with accentuation in the atrio-ventricular grooves. Both auricles were free and considerably dilated. The myocardium of both ventricles was very atrophic. No definite evidence as to etiology was discovered.

Case 11. N. F. This patient was a rabbi born in Russia in 1876. Because of language dif-

ficulties, it was impossible to determine whether any illness suggestive of acute pericarditis had occurred in previous years. He was well until 1947 when there was onset of dyspnea and ankle edema. He was treated with digitalis with benefit. Examination in June, 1950, revealed distended neck veins, blood pressure 160/96, auricular fibrillation, a harsh systolic murmur at the apex, liver margin at the level of the umbilicus, 3 plus pitting ankle edema. X-ray of the chest revealed a dilated superior vena cava, right pleural effusion, and pericardial calcification in the inferior and left borders of the heart. Venous pressure was 280 mm. saline and never was less than 200 mm. when fully digitalized and after mercurial diuresis. Surgery was considered to be inadvisable because of the patient's age.

The patient was admitted to the hospital in August, 1950 for treatment of his moderately refractory edema. He died unexpectedly in his sleep a few days after admission.

Case 12. M. T. This colored female patient born in 1899 had spring and summer asthma from 1939 to 1945. Between 1943 and 1948 she was followed in a city clinic because of a lesion in the apex of the left lung which was believed to be quiescent. Several members of the family had died of tuberculosis. In June, 1948, there was onset of weakness, easy fatigability, heavy feeling in the abdomen, attacks of coughing with vomiting, and ankle edema. Examination in December, 1948, revealed blood pressure 110/80, palpable apical impulse and liver to the level of the umbilicus. Observations of venous pressure varied between 160 and 250 mm. saline. The heart was normal in size with some prominence of the pulmonary artery. Because of continued low-grade fever and tachycardia the patient was transferred to a sanatorium where she remained for six months. In June, 1950, it was discovered that the patient had felt quite well since discharge from the sanatorium in September, 1949. She had, however, continued to have exertional dyspnea and ankle edema as well as "bloating of the stomach". There was distention of the neck veins, an accentuated P2 and a scratchy systolic sound over the left mid-precordium. The liver extended 3 cm. below the right costal margin. X-ray revealed no pericardial calcification. The heart was normal in size with prominence of the pulmonary artery. Venous pressure was 280 mm. saline. Operation was postponed because of the patient's age and relatively insignificant symptoms.

Case 13. J. H. This white male patient born in 1925, first had manifestations of constrictive pericarditis in 1941 when enlarged neck veins were noted. His original admission for pneumonia of the right lower lobe due to type 2 pneumococcus was in November, 1946. The classic signs of constrictive pericarditis were discovered. Jaundice accompanied the pneumonia. There was an overactive precordium at the apex where a palpable diastolic impulse was described. The blood pressure was 90/70 with a distinct pulsus paradoxus. The liver was down 2 finger-breadths. There were bilateral varicoceles. There was 2 plus ankle edema and questionable ascites. Venous pressure before the first operation was 360 mm. saline and the circulation time (Decholin) 25 seconds. Total proteins and A/G ratio were normal. At one time the prothrombin time was 52 seconds (less than 25% of normal). BSP retention in 30 minutes was 44% and the serum cholesterol was 83. EKG revealed T2 and 3 inverted, T4 biphasic. X-ray of the chest revealed the heart to be at the upper limit of normal for size. There was linear calcification in the left border. On January 11, 1947, the first pericardectomy was performed by Dr. Alfred Blalock. The incision was made to the right of the sternum with removal of several costal cartilages. A greatly calcified pericardium was encountered. The right auricle and right ventricle were decorticated. One week following the procedure the venous pressure was 170 mm. saline, and the liver had diminished somewhat in size. However, the venous pressure remained between 170 and 250 mm. saline. Therefore, on July 28, 1947, a second operation was performed. On the left, costal cartilages 3 to 6 were removed and the left and anterior surfaces of the heart were freed of a heavy calcium deposit. Even after this second operation there occurred no definite improvement in either

venous pressure or the tendency to accumulate fluid. In the three years since the last operation the edema and ascites have become slowly but progressively more pronounced and refractory to treatment. The patient has complained continually of cold hands and feet, and there is at times obvious cyanosis of the nailbeds and lips. The venous pressure remains over 200 mm. saline at all times. There is no evidence of a specific etiology in this case, although in August, 1949, he developed a chronically draining sinus in the left precordial incisional scar. No acid fast bacilli have been identified in the draining material. Exploration of the sinus tract in July, 1950, suggested that it might be kept open by a sequestrum of calcified pericardium. The sinuses continued to drain and the patient had persistent fluid accumulation requiring mercurial diuretics at least twice weekly. For this reason a third pericardectomy was performed on September 14, 1950, by Drs. Blalock and Bahnson, using an anterior incision in the fourth interspace on the left. Considerable reformation of pericardial scar was discovered. The right auricle, right ventricle, and left ventricle were decorticated in a very extensive fashion. Postoperatively the venous pressure remained elevated, the sinus tracts re-opened, and the manifestations of chronic congestive failure continued unabated.

The patient was re-studied extensively in August, 1951. Normal venous pressure, normal liver size, and absence of edema led us to believe the patient may at last have attained a clinical cure. He is seeking employment for the first time in many years.

Case 14. G. V. S. This is a white female patient born in 1929. At age 5 there occurred a bout of tonsillitis, accompanied by "smothering spells" causing the child to sit up at night. A physician stated at that time that the liver was enlarged. At age 11 ascites developed together with aching epigastric pain and nausea about once a week. At age 12 face edema in the morning was noted as well as epigastric pain on exertion. "Smothering" with exertion had its onset at age 14. Physical examination revealed full fundal veins, absent precordial impulse, a diastolic sound (described as a presystolic murmur by some), an accentuated second pulmonic sound, blood pressure 108/64, questionable pulsus paradoxus, liver down 4 finger-breadths, spleen down 1 finger-breadth. EKG revealed flat T-waves in all leads. X-ray revealed a moderate amount of pericardial calcification. On August 3, 1943, the first operation was performed by Dr. Alfred Blalock. The ends of ribs 4, 5 and 6 on the left and the corresponding costal cartilages were removed. Grossly the heart was bound in a constricting process which appeared to be caseous in places. Because of the "caseous" material, particularly on the right, no attempt was made to expose the venae cavae. Histologically, hyaline scarring and focal calcification were described, but no caseation. The venous pressure was not reduced following operation, although systolic blood pressure did rise to 125 mm. Hg. Exercise tolerance was moderately limited and mercurial diuretics were required for control of fluid accumulation. Because of failure to attain more improvement a second pericardectomy was performed by Dr. Alfred Blalock on August 6, 1947, through a median sternotomy incision. A very extensive decortication was performed freeing especially the right side of the heart and venae cavae. Following this operation, too, the venous pressure did not drop significantly. In November, 1948, the patient gave a history of excellent exercise tolerance. However, the liver was down 4 finger-breadths and the venous pressure was 210 mm. saline; no peripheral edema had been noted. When restudied in May, 1950, the patient was found to be relatively asymptomatic except for RUQ pain and slight ankle edema occurring with upper respiratory infections and just prior to menstruation. Moderate acrocyanosis was observed during an upper respiratory infection. Venous pressure was 200 mm. and she was negative to skin test with O.T. 1:100 (P.P.D., second strength, was negative in 1943). The improved functional capacity was maintained until March, 1951, when ascites and edema of the legs reappeared coincident with a bout of bronchopneumonia. Diuresis was accomplished only

with some difficulty. The venous pressure was consistently over 210 mm. saline. A third pericardectomy was performed on May 1, 1951, through a left anterolateral chest incision in the fourth interspace. Dense scar tissue with calcification encased the heart. Most of the calcified tissue lay posteriorly. A very liberal decortication was performed. Three weeks later the venous pressure was 125 mm. It is believed that she has been much improved by operation, although it is still too early to be certain about long-term results. In October, 1951, the patient was well and active.

Case 15. P. H. This is a white female patient born in 1920. In June, 1947, while she was working in the fields, pain began in the right upper quadrant and radiated downward. Appendectomy was performed. In January, 1948, the right upper quadrant pain became worse and was accompanied by nausea and vomiting. Laparotomy at that time revealed an enlarged liver which, however, was histologically normal. In April, 1948, the principal physical signs were high right diaphragm, greatly distended neck and arm veins, absent precordial impulse, distant heart sounds, liver reaching to the iliac crest, minimal or no ascites and no leg edema. Venous pressure was 275 mm. saline. The only abnormality of liver function was a prothrombin time of 29 seconds. On x-ray the heart was but little enlarged. The superior vena cava was impressively dilated. Operation through a median sternotomy was performed on May 10, 1948, by Dr. Alfred Blalock. A dense fibrous process, one centimeter thick in places, involved the right auricle and right ventricle. A lappet of dense adherent pericardium extended from the diaphragmatic surface upward about one-half inch onto that portion of the left ventricle which could be visualized. The pericardium was densely adherent over the left anterior descending coronary artery and could not be resected at that point. Immediately following operation the venous pressure was 135 mm. saline and it fell quickly to normal thereafter. In November, 1948, venous pressure was 100, the liver was down only 1 finger-breadth and the patient was asymptomatic.

Case 16. M. C. This is a white male patient born in 1928. In December, 1944, he suffered a grippe-like illness characterized by chills and joint pains. In May, 1945, there was onset of swelling of the ankles and abdomen. The patient complained bitterly of coldness, cyanosis, and pain of the feet on relatively slight exposure to cold. Small black areas appeared on the feet, and he was admitted to another hospital for "frost-bite". There was story of fainting following exertion in April, 1943, at which time a physician told him he had low blood pressure. When studied in 1945 the important findings were blood pressure 100/74, distended neck veins with prominent pulsations, a Wenckebach sign (35), distant heart sounds, left pleural effusion, ascites, liver down 4 finger-breadths and moderate ankle edema. Laboratory findings included a venous pressure of 170 mm., negative first and second strength P.P.D., polycythemia (r.b.c. 7.0 million, hgb. 17.5 gm.). On November 13, 1945, pericardectomy was performed by Dr. William P. Longmire, Jr. The left ribs 3 to 5 were resected, and a densely fibrotic process was found involving all aspects of the heart visualized. A large area of both left and right ventricles was decorticated. Following operation venous pressure fell to 75 mm. saline, and fluid accumulation ceased. He was well and doing hard farm work when seen in March and October, 1946. When restudied in December, 1948, the venous pressure was 95 mm. saline; the liver was at the right costal margin. However, on examination of the heart the second pulmonic sound was found to be reduplicated, and there was a mid-diastolic sound at the apex suggesting mitral stenosis to one observer. On auscultation inspiration was conspicuously cog-wheel in character over both sides of the chest but especially on the left. The patient had been actively engaged in farm work when seen in 1951.

Case 17. E. C. P. This white male patient, born in 1895, from July to October, 1945, had a fever of undetermined cause accompanied by night sweats, epigastric fullness and weight loss. Shortly thereafter there was onset of ankle edema, ascites and paroxysmal coughing when

lying on the right side. Physical examination in 1945 revealed marked venous distention, limited chest expansion, particularly on the right, blood pressure 110/85, pleural effusions, ascites, leg edema and liver down four finger-breadths. Venous pressure was 200 mm. saline, circulation time 16 seconds (Decholin). X-ray showed moderate enlargement of the heart, a high right diaphragm, and pleural thickening. On November 7, 1946, pericardectomy was performed by Dr. Alfred Blalock through an incision in the fourth right interspace. The right auricle and ventricle were decorticated. The venous pressure fell to normal in the first post-operative week. On examination in November, 1948, the heart sounds were found to have a peculiar scratchy pericardial quality. Venous pressure was 100 mm. saline. In May, 1950, it was learned that the patient had been working full time as a post office clerk without any difficulty whatever. Heart sounds were perhaps somewhat muffled but otherwise not remarkable. The liver was not enlarged. The etiology in this case was clearly tuberculosis. The scar tissue removed at cardiac decortication contained tubercles. His first wife died of tuberculosis, and in July of 1948 the patient developed tuberculosis of the right ankle. A lymph node from the right inguinal area showed tubercles. In July, 1951, the patient was still well.

Case 18. B. S. This is a white female patient born in 1908 who at the age of 7 had pain in her knees. At the age of 14 she was told she had a "bad heart". From the age of 18 on she required two pillows for sleeping and had fairly marked exertional dyspnea. Her first pregnancy was terminated successfully by Caesarian section at age 27. In 1940 ascites with slight ankle edema appeared, and the patient required 17 or 18 paracenteses in a 3 months period. The significant findings on examination in that year were generalized venous distention, right hydrothorax, absent precordial impulse, reduplicated first sound or presystolic gallop at the apex, liver down 3 finger-breadths, marked ascites, blood pressure 104/80, venous pressure 275 mm. saline. On August 28, 1940, the first operation was performed by Dr. W. F. Rienhoff, Jr. On the left the 3rd and 4th costal cartilages and a portion of the sternum were removed. Numerous adhesions were discovered between the parietal and visceral pericardium and these were easily freed with the finger. A portion of parietal pericardium was resected. Following this procedure the venous pressure remained elevated. Consequently on November 18, 1940, Dr. Rienhoff opened the right side of the chest by an arcuate parasternal incision. The great veins were decorticated. Venous pressure on February 8, 1941, was 165 mm. saline. Throughout a six month hospitalization the patient ran a persistent low grade fever which was not satisfactorily explained. Numerous tuberculin skin tests were negative. A story was elicited of frequent episodes of eczematous eruption over the nose and at one time over the entire body.

When examined in 1943 the patient was able to do the work of a farm wife and sleep on one pillow. The right chest was nearly immovable. The venous pressure was 175 to 200 mm. saline. In the interval until 1949 the patient had felt quite well and had been able to work hard. She had noted ankle edema and dyspnea with increased salt intake. When studied in 1949 significant findings included a twin pregnancy, distended neck veins, pitting edema of the legs, venous pressure 290 mm. saline, vital capacity 1.1 liters in 3 seconds. With digitalization and bed rest the venous pressure returned to normal and the patient was delivered of healthy twin infants at term without complications.

Case 19. P. E. G. This white female patient born in 1916 was in contact with two maternal aunts and a maternal uncle, all of whom died of tuberculosis. At the age of 10 she noted that she had to drop out of games because of dyspnea. Ankle edema progressing to anasarca began at age 12. Digitalis was administered without benefit for about 10 years beginning at the age of 12. In 1941 when the patient was studied at the Peter Bent Brigham Hospital by Dr. C. S. Burwell the principal cardiac findings were a systolic retraction of the left precordial

costal cartilages, a scratching mid-systolic sound, and in the first half of diastole a prominent third sound which at the apex was louder than the first and second sounds. Venous pressure was 215 mm. saline, and total proteins were 3.9 gms. There was pericardial calcification located principally in the atrioventricular sulcus. On November 4, 1941, operation was performed by Dr. Elliot C. Cutler using an arcuate left parasternal incision. Only a partial decortication was possible because of adherence of the pericardial scar to the coronary arteries. Following operation there was moderate but persistent improvement. She has been studied at frequent intervals during the nine years since operation. The loud protodiastolic sound has persisted. Venous pressure has been between 140 and 200 mm. saline. The tendency to accumulate fluid has continued but has been held in abeyance by careful salt restriction and high protein intake. In June, 1950, the neck veins were moderately distended, there was a very prominent early diastolic sound, the liver was 1½ finger-breadths below the right costal margin and there was slight pitting ankle edema. Total serum proteins were 5.6 gms.% with an albumin of 2.5 gms.%. Venous pressure was 170 mm. saline. One pregnancy had been successfully completed in January, 1949, and the patient was again pregnant in June, 1950. This terminated in spontaneous abortion following which the patient felt subjectively improved.

Case 20. E. C. This white male patient, born in 1928, was exposed to tuberculosis as his mother died of this disease when he was 3 years old. At the age of 2½ years he developed tuberculosis of the right hip which required prolonged hospitalization. While the patient was in a body cast at the age of 15 years, dyspnea was first noted. On examination in 1945 findings included blood pressure 107/80, absent apical impulse, split first sound, tic-tac rhythm, marked tachycardia (persistent for about one year), liver down 3 to 5 cm., palpable spleen, ascites and sacral edema. Venous pressure was 260 mm. saline, total proteins 4.81 gms. with 2.25 gms. albumin, P.P.D. positive in the first strength. On April 4, 1945, pericardectomy was performed by Dr. Alfred Blalock through a curved left parasternal incision with removal of costal cartilage 2 to 6. Mainly the right ventricle was decorticated. The pericardium was very adherent particularly along the left anterior descending coronary artery. Histologically the surgical specimen showed only scarring and thickening of the pericardium. By May 2, 1945, serum proteins had returned to normal, but venous pressure was still 230 mm. saline, and the liver was down 3 finger-breadths.

When re-examined in 1950 it was found that the patient had been very well since operation. There was no edema and no dyspnea. His activity had been limited only slightly and that by his orthopedic deformity. Physical examination revealed normal cardiac action as visualized and palpated through the defect in the bony thorax, liver not palpable, no edema, cog-wheel inspirations over the left hemi-thorax only. Venous pressure was 140 mm. saline. On fluoroscopy the heart was normal in size and appearance. There was during inspiration a tugging of the left diaphragm by the heart as a result of an inferoposterior adhesion.

SOME LABORATORY OBSERVATIONS

Cardiac catheterization

Sixteen cardiac catheterizations[1] were performed in thirteen patients in this series. The right ventricular pressure recordings were available for review in eleven catheterizations in ten patients. One of the tracings was recorded with a Hamilton manometer, six with a Statham strain gauge and five with a San-

[1] Most of the catheterizations were performed in the laboratory of Dr. Richard J. Bing, to whom the author is indebted for permission to include the data here.

born Electromanometer. All but one of the right ventricular pressure tracings showed an early diastolic dip followed by a rapid rise to a diastolic plateau at a high pressure level (as high as 32 mm. Hg in Case 2). All the patients in whom these characteristic pressure curves were recorded either were pre-operative and had a "flat-top and V" pattern by electrokymography (2) or still had clinical evidences of constriction with persistence of the characteristic EKY pattern after operation. In brief, the correlation between the right ventricular pressure pattern and the electrokymographic pattern was close. Unfortunately, however, no pressure tracings are available in patients who had obtained clinical and EKY improvement from operation (2). Hansen and co-workers (3) have described cases in which the diastolic "dip" disappeared following pericardectomy. Case 12 who did not show the characteristic pattern was catheterized before development of the full syndrome of cardiac constriction.

In describing the characteristic right ventricular pressure curve[2] in constrictive pericarditis, both Bloomfield (4) and Hansen (3, 5) emphasized that it is not specific since right sided heart failure of any cause may show an early diastolic "dip" and a diastolic plateau. Richards (6) published such curves in cases in failure and normal curves after compensation. Wood and co-workers (7) published tracings from a case of constrictive pericarditis showing an early diastolic "dip" followed by a diastolic plateau. Two tracings recorded by means of strain gauges were published and these authors interpreted the early diastolic "dip" as a distortion produced by a low frequency recording system since the early diastolic "dip" was less conspicuous (but still present) in recordings by an instrument of higher frequency response. Sawyer (8) has found this pattern quite consistently in constrictive pericarditis but also recorded it in a case of myocardial fibrosis. Hansen (9) likewise found it in one case of myocardial fibrosis and we have recently had the same experience.

Wiggers (10) believes the small early diastolic "dip" in right ventricular pressure curves recorded by cardiac catheterization even in normal individuals is a "low frequency artefact." The inference would appear to be that all such "dips" are artefacts. As stated by Katz (11) in his critical review, the "dip" was described by early workers using cruder recording apparatus and was attributed to a suction action of the relaxing ventricle. It could not be demonstrated in normal animals by more recent workers employing instruments designed according to the principles of Frank.

The presence of a suction action in the normal relaxing ventricle is probably disproven. There is at least a remote possibility that ventricular suction occurs in constrictive pericarditis. Retraction of portions of the chest wall with systole is a conspicuous sign in some patients, e.g., Case 7. Elastic recoil of the rigid

[2] For an example of the characteristic pressure curve, see Figure 9 in an accompanying paper (2).

pericardial case or of the thoracic cage to which it may be adherent might conceivably result in a suction effect.

TABLE 1

Findings of Cardiac Catheterization

NO.	CASE	TYPICAL RT. VENTRICULAR PRESSURE CURVE	PRESSURES (MM. HG.)*				C.I.	ARTERIAL % O_2 SAT.
			RA	RV	PA	PC		
1*	1. (S. W. A.) 10-8-48		28/21	37/20†			3.05	97.4
2*	2. (R. McA.) 1-17-49	Yes (S. G.)‡	37/31	53/32	43/17		2.04	95.0
3*	2. (R. McA.) 5-3-49		10/6	41/8	33/18		3.78	
4	3. (A. N.) 8-30-49	Yes (EMN)		50/20			2.50	90
5*	5. (C. L. M.) 8-10-50	Yes (S. G.)		32/14			2.28	96
6*	6 (L. N.) 12-16-49				42/26		1.27	87
7*	7. (W. B.) 9-7-50	Yes (S. G.)	36/28	57/30			2.06	95
8*	7. (W. B.) 10-9-50		7/3		18/8		2.45	
9	8. (J. M.) 12-29-49	Yes (EMN)	14/7	35/12	38/18	12	2.09	85
10*	9. (N. D.) 5-11-49	Yes (S. G.)	17/11	31/13	24/13		1.9	98
11*	9. (N. D.) 11-22-49	Yes (S. G.)	19/10	30/6	30/13	10	3.91	91
12*	10. (W. M.) 5-25-50	Yes (S. G.)	18/12		42/18	24	2.73	87
13*	12. (M. T.) 9-17-48	No (S. G.)	30/26	31/16	31/16		2.0	
14	13. (J. H.) 4-27-50	Yes (EMN)	28/17 (mean 24)	50/15 (mean 35)	45/28	28	2.0	100
15*	14. (G. V. S.) 6-4-47	Yes (Ham.)	33/28	49/29	44/31		2.10	96
16*	15. (P. H.) 4-9-48						2.14	96

* Study performed in laboratory of Dr. Richard J. Bing.

† RA = right auricle. RV = right ventricle. PA = pulmonary artery. PC = pulmonary "capillary". (In reporting ventricular diastolic pressure the level of the diastolic plateau was used rather than the pressure at the nadir of the early diastolic "dip".)

‡ S. G. = Statham strain gauge. Ham. = Hamilton manometer. EMN = Sanborn Electromanometer.

The mechanism of the right ventricular pressure pattern is not entirely clear. However, until further evidence to the contrary is available, the writer prefers to consider the "characteristic" right ventricular pressure curve as a reflection

of an actual cardiodynamic event. The early diastolic "dip" corresponds closely with anomalous cardiodynamic phenomena recorded by sound tracings (2, 16) electrokymograms (2), and ballistocardiograms (12). That the pressure pattern may be bona fide is further supported by the finding of Dr. Hansen (3) while working at the Johns Hopkins Hospital. In Case 7 early diastolic "dips" were recorded from both left and right ventricles through needles introduced directly into the ventricle at operation. Furthermore, the early diastolic dip was of roughly the same absolute amplitude in the two ventricles.

In constrictive pericarditis the right auricular pressure pulse is wider than it is normally, that is, the auricular pulse pressure is greater. Furthermore, at the time of ventricular filling there is a deep V-shaped excursion of the auricular pressure curve. The complete curve is roughly M-shaped. The wide pulse pressure is probably explicable on the basis of the electrokymographic findings (2). With auricular contraction pressure rises higher than usual since ventricular filling is already complete. With rapid ventricular filling the auricular pressure drops relatively low for a brief period. The right auricular pressure curve of constrictive pericarditis provides two bits of evidence suggesting that the "characteristic" ventricular pressure curve is bona fide (cf. (2) for tracings):

(A). A "dip" occurs in the right auricular pressure curve at the same time as in the right ventricular pressure curve;

(B). The auricular and ventricular "dips" are of roughly identical shape and absolute amplitude.

The elevated "pulmonary capillary" pressure in those instances where it was determined indicates the importance of the factor of left ventricular constriction in these cases. This finding is in accord with those of Burwell (37).

Angiocardiography

Angiocardiography was performed in four of these cases (#1, 3, 8, and 15). In none was a localized inflow obstruction demonstrated. Sellors (41) expresses the opinion that the venae cavae "can be reduced to the diameter of little more than a lead pencil without interfering with an efficient circulation, providing that the ventricles are sound." The positive findings of angiocardiography included: (1) dilated superior vena cava (all cases); (2) thickening of the wall of the heart on the right border (right auricle) in Cases 1 and 15; (3) close apposition of the opacified right ventricle to the sternum as seen in lateral view (i.e. obliteration of the retrosternal space) in Cases 1, 8, and 15; (4) dilated main pulmonary artery in Case 8; and (5) dilated left auricle in Case 8.

Renal clearances

In seven of these patients determinations were made of glomerular filtration by inulin or thiosulfate clearance, of effective renal plasma flow by para-aminohippurate clearance, and of filtration fraction by derivation. The results

are given in Table 2. The most conspicuous feature is a consistent elevation of the filtration fraction. Further elevation of this value with exercise was observed in the two cases in which this was tested. Elevation of the filtration fraction occurs with congestive heart failure due to other causes (13).

TABLE 2

*Renal Clearance Data**

CASE	DATE	GLOMERULAR FILTRATION RATE	RENAL PLASMA FLOW	FILTRATION FRACTION
1. (S. W. A.)†	10–6–48	127	610	.21
		168	832	.20
		103, 126 exercise on treadmill	390, 445	.26, .28
		133	520	.26
		150	557	.27
		124	458	.27
3. (A. N.)	9–5–49	104	318	.33
		82	259	.27
9. (N. D.)	5–13–49	145	473	.29
		136	259	.27
12. (M. T.)†	9–9–48	73	168	.44
		73	170	.46
		76	167	.47
		78	135	.58
		69	215	.32
13. (J. H.)	6–7–50	125	468	.27
		107	344	.31
14. (G. V. S.)†	5–29–47	110	364	.30
15. (P. H.)†	4–19–48	82	310	.27
		76	260	.29
		87	264	.33
		78, 61 exercise on treadmill	266, 194	.29, .32
		80	232	.35
		83	242	.32
		73	249	.34

* All 12 to 16 minute periods. Consecutive periods when more than one given.

† Data provided by Dr. Elliot V. Newman.

GENERAL CLINICAL COMMENTS

Etiology

In eight of these twenty cases there was adequate evidence for a tuberculous etiology. The evidence consisted of unusually concentrated and prolonged exposure to tuberculosis or evidence of tuberculosis in the pericardial scar or at

sites other than the pericardium, e.g., bone, lymph node, or lung. The other twelve cases are representative of the majority of cases, in which evidence of a specific etiology is unobtainable. This does not necessarily indicate that tuberculosis is not the cause in most if not all cases. Even the absence of more than non-specific scar at operation or autopsy is no evidence against tuberculosis. A very instructive case in this regard was studied at the Johns Hopkins Hospital over a 20 year period and has been reported elsewhere (19). At various times during this period of observation he had clinically typical tuberculous pericarditis with effusion, cervical lymphadenopathy which was proved to be tuberculosis by biopsy, active pulmonary and mediastinal tuberculosis, pleural effusion with acid-fast bacilli demonstrable in the fluid, and presumably tuberculous chorioretinitis. In 1935 he developed the full-blown syndrome of chronic constrictive pericarditis with calcification by x-ray. In Cleveland on July 25, 1936, Dr. Claude S. Beck performed cardiac decortication; in spite of the unequivocal past history, only nonspecific hyalinized and calcified pericardial scar was found. Case 20 is very comparable. There was undoubted tuberculosis of the hip, but the pericardial lesion was only non-specific scar at the time of operation.

There is a significant number of cases with typical constrictive pericarditis in whom the tuberculin skin tests are repeatedly negative. Cases 14, 16, and 18 in this series and patient C. W. described later are examples of this. Speculation as to the etiology of these cases I will leave to others. It has not been possible to discover in the pathology files of the Johns Hopkins Hospital a case of constrictive pericarditis conceivably due to disseminated lupus erythematosus (42).

Trauma should not be overlooked in the etiology although this cause has never been proved unequivocally. Blunt trauma to the chest, such as the "steering wheel injury" of Beck (20), can produce hemopericardium with subsequent organization and calcification and, conceivably constriction. It is very likely that Case 5 was due to trauma because of the finding of a subdural hygroma-like cyst between the heart and the sternum and because of the history of profound although indirect trauma two years previously. By analogy to subdural hygroma the abrupt and relatively late onset of symptoms is readily explicable. The subjective complaint of "fullness of the head" in the supine position was quite out of proportion to that usually observed and may be explained by the nature and position of the pericardial cyst in this case. Mortensen and Warburg (17) report a case of this condition due to trauma. It is possible that trauma to the chest may precipitate constrictive pericarditis by causing rupture of tuberculous lymph nodes into the pericardium with subsequent scarring. White and Glendy (21) described what may be such a case: "In one of our 16 cases of Pick's disease a severe blow on the chest preceded the symptoms and signs of a bloody pericardial effusion, which later developed into a chronic tuberculous constrictive pericarditis requiring operation."

The protodiastolic sound

An adventitious sound in early diastole was described at some time in about half the cases of constrictive pericarditis in this series (Fig. 1). Simultaneous recordings of heart sounds and ventricular border electrokymograms conclusively demonstrate that the protodiastolic sound is due to rapid ventricular filling early in diastole and/or abrupt halt in ventricular filling (2).

The protodiastolic sound of constrictive pericarditis was apparently first described by Potain (14) in 1856. Lian, Marchal, and Pautrat (15) wrote about

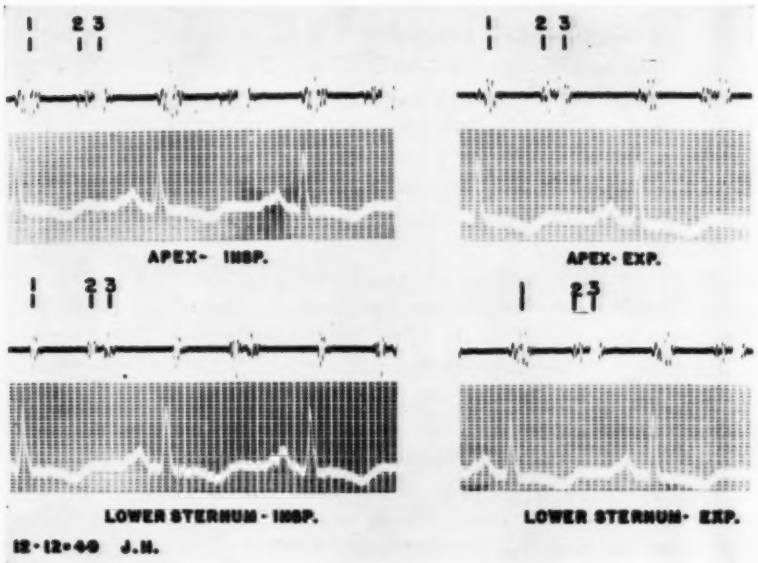

FIG. 1. These phonocardiograms from patient #13 show the prominent protodiastolic sound (marked "3"). At the apex during inspiration and at the lower sternum during expiration the protodiastolic sound is louder than the first and second sounds.

this protodiastolic sound and referred to it as the pericardial protodiastolic vibration to distinguish it from the normal third heart sound and protodiastolic gallops. (This terminology has advantages since the term "gallop" has well established diagnostic and prognostic connotations.) They believe that it occurs only with pericardial calcification. This indeed appeared to be almost true in our studies as well. Only Case 6 had a definite protodiastolic sound in the absence of pericardial calcification. Why calcification should be necessary for the development of the extra sound is not clear since calcification is not essential to its explanation (2).

Mortensen and Warburg (17) found a "mesodiastolic gallop" in 16 of 25

cases. Paul, Castleman, and White (18) observed "a distinct third sound" in 15 of 53 cases.

Serum proteins

Total serum proteins and albumin-globulin ratio were determined at least once in all twenty cases of constrictive pericarditis. Cases 6, 16, 19 and 20 had serum albumins of 3.0 gms. or less. Cases 13 and 14 had serum albumins between 3.0 and 3.5. All six of these cases had had their disease from at least the early teens. Pediatricians in particular (22, 23) have emphasized the serum

FIG. 2. The "sugar-coated" liver in a dog with chronic constrictive pericarditis produced by cellophane around the heart.

protein changes in the syndrome of chronic constrictive pericarditis. Growth may place demands on the congested liver which it cannot fulfill but which are not present in the adult. Another possible factor may lie in the fact that few of these patients had any abdominal paracenteses. In the patients who were tapped, paracenteses were performed only two or three times at widely spaced intervals. Regeneration of serum proteins may occur very rapidly after operation as seen in Case 6.

The liver

Five patients in this series had hepatic friction rubs synchronous with respiration. Palpation of the enlarged liver in one of these cases produced a pecu-

liar sensation to the examining hand somewhat resembling subcutaneous emphysema. This is the clinical analogue of the *Zuckergussleber* of Curschmann (24). A dog[3] in which the clinical syndrome of constrictive pericarditis was produced by wrapping the heart in cellophane showed at autopsy six months later marked "sugar coating" of a much enlarged liver (Fig. 2). Histologically this coating was fibrin overlying a collagenous thickening of the liver capsule (Fig. 3). Blalock and Burwell (25) described "hyperplastic peritonitis" in their dogs with aleuronat pericarditis. In patients the hepatic friction rub tends to occur post-operatively while the liver is shrinking in size and may be a source of much discomfort to the patient and concern to the physician. It appears, however,

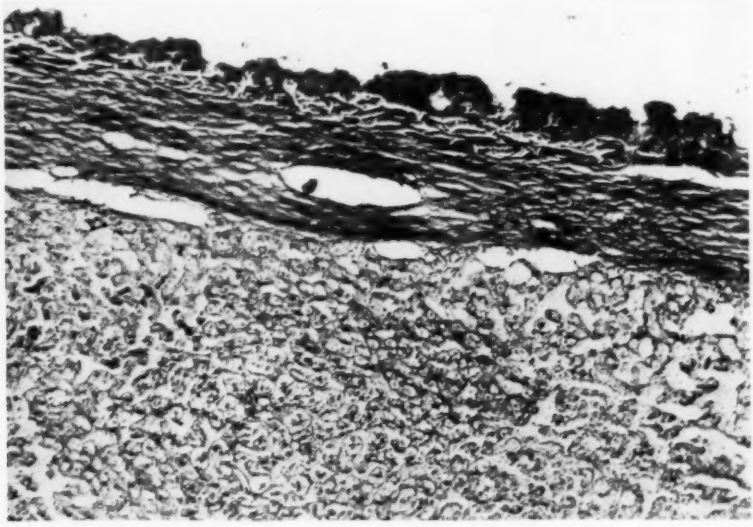

FIG. 3. Histological appearance of "sugar-coated" liver shown in Figure 2. There is fibrous thickening of Glisson's capsule with much overlying fibrin.

to be of no serious import and most of the patients who have shown it have had clinical cures.

Chest x-rays

The dilated superior vena cava is an impressive feature of the chest x-rays of these cases. Before operation it was present in some degree in all twenty cases of the constrictive syndrome. Venous pulse type electrokymograms (2) are usually easily recorded from the dilated structure. In few other cardiac conditions does elevated venous pressure persist for such a long period of time.

[3] Reported through the courtesy of Dr. James O. Davis of the National Heart Institute.

As a result the elasticity of the vena cava is lost just as is the case with the neck veins. A dilated superior vena cava with little or no enlargement of the heart is highly suggestive of constrictive pericarditis. Among others, Kerley (26) and Friedberg (27) have remarked on this phenomenon.

Calcification was demonstrated roentgenographically in 10 of the 20 cases of constrictive pericarditis in this series. This is approximately the percentage of calcification found in the series of 53 cases published by Paul, Castleman, and White (18). The calcification was always predominant on, or limited to, the diaphragmatic aspect of the heart. Presumably this is due to sedimentation of inflammatory elements which later become calcified. The calcification also tends to be dense in the atrio-ventricular grooves. The apex is likely to be free of calcification.

Respiratory function

Impaired respiratory function of a type pointing to primary pleuro-pulmonary disease is present in most cases, outstanding in some. They usually have thickened pleura by x-ray, reduced vital capacity, impaired chest expansion. Most cases, one must conclude, have some degree of constrictive pleuritis in addition to constrictive pericarditis. An extreme example of this association was reported by Burwell and Ayers (28). Recently at the Johns Hopkins Hospital a case of constrictive pericarditis with calcification of the pleura as well as the pericardium has been studied.

Cyanosis

Cyanosis with arterial oxygen unsaturation at rest is uncommon but not unknown in constrictive pericarditis (29, 30, 31). Mortensen and Warburg (17) reported cyanosis in 18 out of 25 cases; there were no data on arterial oxygen saturation. Cases 7, 9, 12, 13, and 16 were cyanotic at rest and Case 14 became cyanotic with even mild upper respiratory infections. (In Case 10 the cyanosis was probably due to methemoglobin which was found to represent 10% of the total hemoglobin and which may have been produced by mannitol hexanitrate.) Cases 7 and 16 had polycythemia as well as cyanosis. Friedberg (31) suggests that the probable cause is "associated pleuropulmonary disease or peripheral venous stasis."

Syncope

Syncopal attacks occurred on at least one occasion in Cases 2, 10, and 16. In all three cases the syncopal attacks occurred during exertion. Since these cases are prone to auricular arrhythmias, a bout of tachycardia or cardiac standstill preceding change in mechanism may be the cause. However, in Cases 10 and 16 fibrillation or other arrhythmia have never been observed. Failure of the cardiac output to increase adequately with exercise (31) is probably a more likely

explanation for the syncope. In Case 2 syncope occurred during electrokymography (2). When the patients hold their breath, as is required in this procedure, they frequently perform a Valsalva maneuver. Syncope occurs in cases of superior vena cava obstruction when venous return through what channels remain is reduced by some factor such as the Valsalva maneuver (32). These observations suggest that straining may be a factor in the syncope of constrictive pericarditis.

Simulation of mitral stenosis

Physiologically and sometimes roentgenologically constrictive pericarditis can very closely simulate mitral stenosis. It is clear that from the physiologic standpoint it makes no difference whether the left ventricular filling is impeded by narrowing of the mitral orifice or by a decrease in diastolic capacity of the ventricle itself. In both conditions a high pulmonary "capillary" pressure is recorded by catheterization. Case 8 (J. M.) had in addition to an elevated pulmonary "capillary" pressure a mammoth left auricle presenting far over on the right side of the heart. Others of these cases, e.g., Cases 2 and 7, had lesser degrees of left auricular enlargement. Not included in this series are two Johns Hopkins Hospital cases of constrictive pericarditis who demonstrated left auricular enlargement to a most pronounced and confusing degree. C. W., a 22 year old white male patient, had the typical history and physical and x-ray findings of constrictive calcific pericarditis. In addition there was a large dog-ear-like mass projecting from the mid portion of the left border of the cardiovascular silhouette. Exploration which was performed because of suspicions of tumor disclosed a greatly dilated left auricular appendage. R. S., a 19 year old colored male patient who was likewise a classic case of constrictive pericarditis, showed radiographically great enlargement of the left auricle to the right and posteriorly displacing the esophagus and left main bronchus. The main pulmonary artery was very prominent due apparently both to dilation and to displacement by the large left auricle. These findings were confirmed by angiocardiography and by surgical exploration at the time of pericardectomy.

Enlargement of the left auricle is clearly demonstrated in x-rays published by White (33). Involvement of the left side of the heart in constrictive pericarditis has been emphasized by White, Alexander, Churchill, and Sweet (34), and by Sawyer (8). Rarely the characteristic auscultatory and cardiodynamics changes of mitral stenosis may be produced by penetration of the atrio-ventricular fissure by the fibrosing and calcifying process with involvement of the mitral ring (16, 38).

One physiologic distinction between mitral stenosis and constrictive pericarditis lies in the response of cardiac output to acceleration of the cardiac rate. In mitral stenosis cardiac output bears, within limits, an inverse relationship to cardiac rate; in constrictive pericarditis the relationship is usually a direct one (39).

Constrictive pericarditis may simulate tricuspid stenosis by virtue of the presence of a presystolic or atrial liver pulsation as pointed out by Wenckebach (35). The fact that the capacity of the ventricle has been reached when the auricle contracts is presumably the mechanism (2).

Results of pericardectomy

Of the twenty cases of constrictive pericarditis in this series seventeen have been subjected to at least one pericardectomy. Fifteen of the cases have been observed for at least two months following operation. The results of operation are given in Table 3. Based on this experience it is the opinion of the writer that every case of constrictive pericarditis with the probable exception mentioned below should be subjected to pericardectomy as soon as the diagnosis is established, active tuberculosis excluded or at least controlled with chemotherapy, and the patient in as good a physical condition as he can be expected to attain. All this assumes, of course, that the patient's symptoms are incapacitation.

TABLE 3

Results of Pericardectomy

POST-OPERATIVE CONDITION	TOTAL NUMBER OF CASES	NUMBER OF INDIVIDUAL CASE IN THIS SERIES
Dead	2	8, 10
Improved	3	3, 13*, 14*, 19
Clinically cured	11	1, 2, 4, 5, 6, 7, 15, 16, 17, 18, 20

* These may be clinical cures.

Two deaths in this series occurred while the patient was on the table undergoing pericardectomy. One patient in this group died without operation. These were the three oldest patients in the series (with the exception of Case 5 which was probably traumatic in origin). In addition these three patients had *Panzerherz*, i.e., very extensive pericardial calcification. Operation should probably not be attempted in individuals with the combination of relatively advanced years and extensive calcification (36). There is likely to be so much myocardial atrophy or coronary artery disease that rupture of the heart or cardiac standstill will occur as was the case in our two patients. By way of contrast cases such as Cases 1 and 5, although in the older age group at the time of onset of symptoms, did not have pericardial calcification and obtained clinical cures from pericardectomy. In the younger age group good results can be expected as a rule in spite of pericardial calcification.

One patient (Case 13) appears to have attained a clinical cure one year after the last of three cardiac decortications. Case 14 has likewise had three operations and although she is now much improved it is still too early to be certain about the ultimate result. What is the cause of the delayed or incomplete success in these fortunately infrequent cases? It seems likely that these cases

have fibrosis involving the myocardium in a too intimate manner to permit complete removal by the surgeon. Isaacs (40) has experimental data in support of this idea.

It will be noted from perusal of the individual case reports that there has been an evolution[4] of incisions or surgical approaches to the pericardium as indicated by Dr. Blalock in the introduction to this group of papers.

SUMMARY AND CONCLUSIONS

1. Clinical features of twenty cases of constrictive pericarditis are presented.

2. A case is presented (Case 5) in which trauma may have been the main etiologic factor in the scarring of the pericardium.

3. Cyanosis, impaired respiratory function, syncope, dilatation of the superior vena cava, serum proteins, simulation of mitral stenosis, and the hepatic friction rub are discussed.

4. Angiocardiography was of no significant diagnostic aid in four cases.

5. Elevation of the filtration fraction was a consistent feature of renal hemodynamics in seven cases studied by renal clearance techniques.

6. In thirteen patients cardiac catheterization was performed. An early diastolic "dip" followed by a diastolic plateau was a consistent feature of the right ventricular pressure curve. All evidence available from these studies is consistent with the view that these recordings represent a bona fide cardiodynamic phenomenon.

7. An adventitious sound in early diastole was present in at least half of the cases in this series.

8. Results of pericardectomy were in general satisfactory. Of fifteen cases who survived operation, eleven attained clinical cures, three were improved, and one unimproved. Two patients died during operation from ventricular rupture and cardiac standstill, respectively. Both patients were over 55 years of age and had very extensive pericardial calcification.

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CHRONIC CONSTRICTIVE PERICARDITIS

II. Electrokymographic Studies and Correlations with Roentgenkymography, Phonocardiography, and Right Ventricular Pressure Curves

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This is a report of electrokymographic findings in twenty patients who had chronic constrictive pericarditis. Clinical aspects of these cases are described in detail in an accompanying paper (1). In addition three patients were studied who had pericardial calcification without the constrictive syndrome. The objectives of these studies were several: (I) Gillick and Reynolds (2, 3) described an electrokymographic (EKY) pattern which from their studies appeared to be quite characteristic of this condition. It was desirable to know how diagnostic this pattern is. (II) The value of electrokymography in evaluating results of operation was studied. (III) Correlative studies with roentgenkymography (RKY) were made to determine to what extent the latter method will demonstrate the characteristic pattern. (IV) Bloomfield et al. (4) and Hansen et al. (5, 6) have reported what they believe to be a fairly pathognomonic pattern of the right ventricular pressure curve in constrictive pericarditis. It was thought that simultaneous recordings of the EKY and the right ventricular pressure curve might shed light on the genesis and significance of each. (V) It was hoped to elucidate the nature of the protodiastolic sound of constrictive pericarditis by determining what is happening mechanically by means of simultaneously recorded electrokymograms.

Electrokymography (7, 8, 9, 10) is a method for detailed analysis of movement of individual points on the x-ray silhouette of the heart and great vessels. For details of the instrument[1] and its use, reference is made to the literature which now records a fairly extensive experience with the method. The technique used for most of the studies has been described elsewhere (10). For the most part the carotid pulse was used for timing purposes. Figure 1 indicates the areas from which recordings of border movement were made as well as the conventions employed in labelling tracings.

Of the twenty cases of constrictive pericarditis five have been studied only pre-operatively, seven have been studied both before and after operation, and

[1] The electrokymograph used in most of these studies was a commercial model manufactured by the Cambridge Company, Ossining, New York.

eight have been studied at least once one to nine years following pericardectomy.

ELECTROKYMOGRAPHIC FINDINGS

The characteristic electrokymographic change of constrictive pericarditis (Figs. 2 and 3) is found in the ventricular border tracings and consists of a simplified pattern of "flat-tops and V's", the two limbs of the "V" representing systolic ejection and ventricular filling respectively, and the "flat-tops" representing diastolic standstill. The characteristics of this pattern are as follows:

(1) There are no secondary curves which ordinarily occur during isometric contraction, early ejection, and isometric relaxation due to positional and rotational movements. This is probably due to the fact that the encased heart is

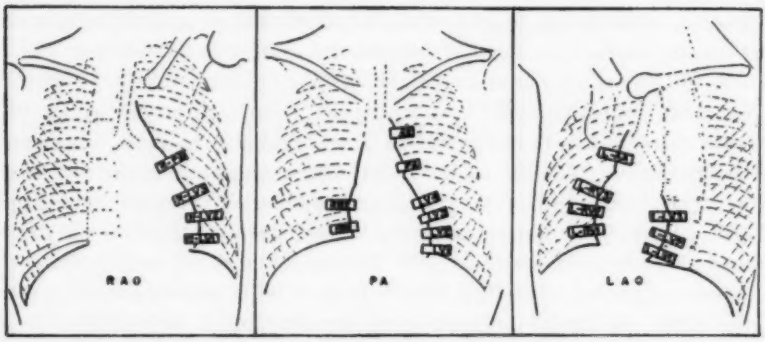

FIG. 1. Indicated here are the positions on the cardiovascular silhouette from which electrokymographic recordings were made and the convention for labeling the individual tracings.

not free to make the extra movements responsible for the inscription of these secondary components.

(2) Ventricular filling is very rapid. The filling limb of the "V" is characteristically steeper than, or at least as steep as, the emptying limb. High atrial pressure on both the right and left side has been an invariable finding of cardiac catheterization in these cases (1) and is probably largely responsible for rapid filling. Elastic recoil of the rigid pericardium and of the thoracic cage structures to which it may be adherent might theoretically produce a rapid outward movement of the ventricular border in early diastole. At present there is no proof of this latter concept. In fact evidence of adhesions to the thoracic cage was notably absent in most of the cases in whom pericardectomy was performed.

(3) Ventricular filling comes to an abrupt end early in diastole and there is standstill of the ventricular border for the remainder of diastole. This is merely

an expression of the long recognized (11, 12) impediment to ventricular filling in this condition.

Other less constant electrokymographic features are as follows: (I) A late systolic plateau indicating, perhaps, an impediment to systolic emptying (Fig.

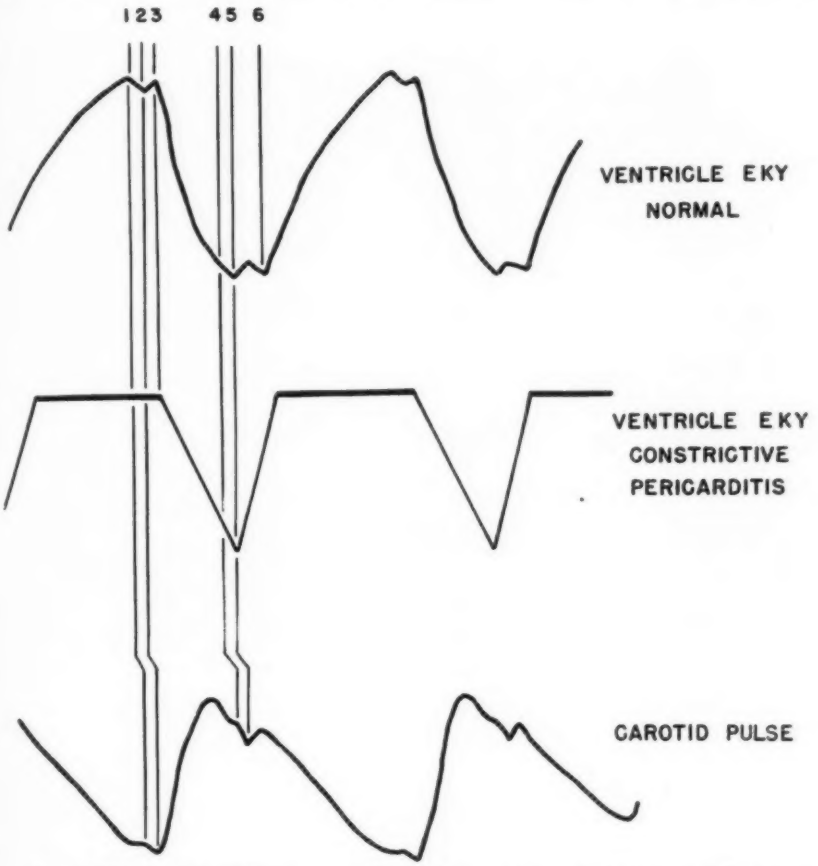

FIG. 2. This is a schematic representation of the normal ventricular border electrokymogram and the "flat-top and V" electrokymogram of constrictive pericarditis with carotid pulse tracing for timing purposes. Phases of cardiac cycle: 1–2, isometric contraction; 2–3, early ejection; 4–5, late ejection ("proto-diastole"); 5–6, isometric relaxation.

5), is most often seen over the upper left ventricular border (LV3 or LV4). According to Stumpf (13) the late systolic or medial plateau was described in roentgenkymograms by Heckmann, who applied to it the same significance we have to the corresponding EKY finding. (II) An "over-shooting" phenomenon

is occasionally seen. This consists of a small rise above the main level of the diastolic plateau occurring at the end of rapid diastolic filling (Fig. 4). (III) In the main pulmonary artery EKY there may be long flat diastolic plateaus which may indicate constriction of the pulmonary artery (Fig. 5). However, it may well be that they are an expression of close relationship between pul-

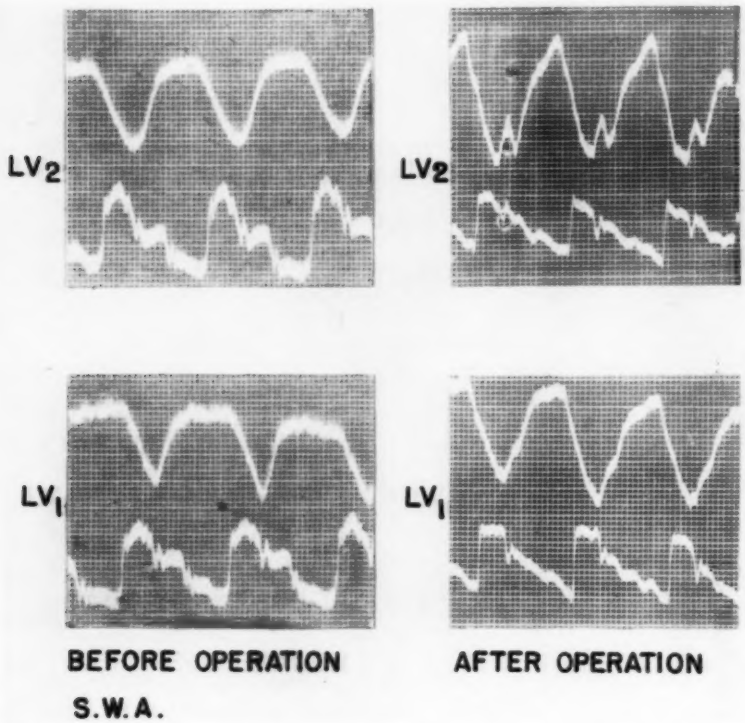

FIG. 3. This patient, case 1 (1), attained clinical cure from pericardectomy. Pre-operative electrokymograms showed an abnormal pattern of ventricular border movement of the "flat-top and V" variety. Post-operatively the pattern returned to normal.

monary 'capillary' pressure, pulmonary artery diastolic pressure, right ventricular diastolic plateau pressure, and mean atrial pressure. (IV) Dampening or obliteration of right auricular pulsations is frequently encountered. (V) Unusually prominent pulsations may be recorded in a dilated superior vena cava. These recordings have the same contour as right atrial pressure recordings (1).

Table I is a tabulation of the electrokymographic findings in this study.

The characteristic "flat-top and V" pattern may not be demonstrable under

two circumstances: 1) tachycardia and 2) concealment of the lower ventricular borders by left pleural effusion and/or high left diaphragm due to ascites. A heart rate of more than about 120 will cause a fusion of the "V's" and obliteration of the diastolic plateau. The typical pattern may be suspected, however, from the presence of a steep filling limb and a V bottom. The typical pattern is always most prominent over the lower borders of the ventricles. Pleural

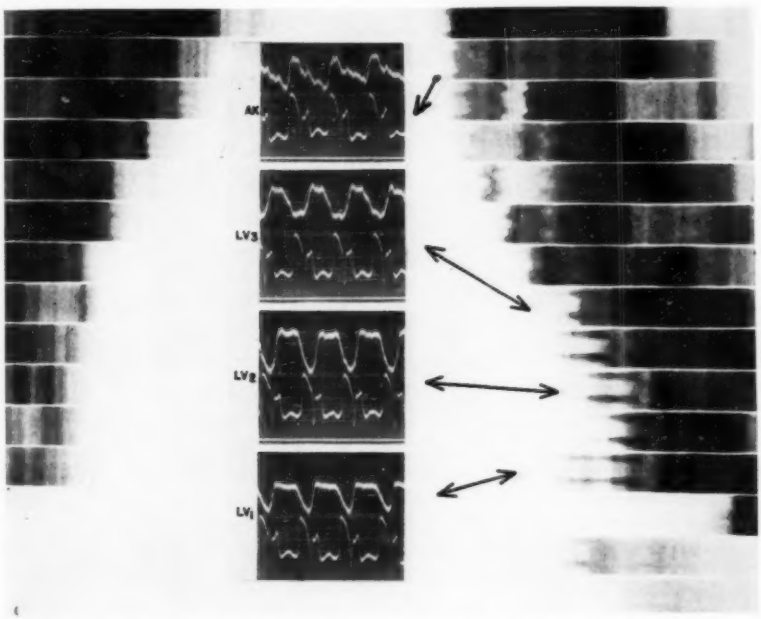

FIG. 4. This patient, case 13 (1), had continuation of manifestations of constriction in spite of two cardiac decortications. Shown here are a roentgenkymogram and, superimposed on it for purposes of graphic visualization, some of the electrokymograms. In each "frame" of the roentgenkymogram border movement is read from bottom to top. The records show the over-shooting phenomenon at the end of rapid ventricular filling.

effusions or a high diaphragm are likely to make it difficult or impossible to study the complete ventricular silhouette.

In the differential electrokymographic diagnosis, bradycardia, as in complete heart block, is the principal condition which can produce "flat-tops and V's" simulating those of constrictive pericarditis (Fig. 7). The distinguishing feature, however, is that bradycardia, unlike pericarditis, produces a filling limb less steep than the emptying limb. Furthermore there are likely to be secondary waves in bradycardia and none in constrictive pericarditis.

A possible source of error to be avoided is having the small segment of the

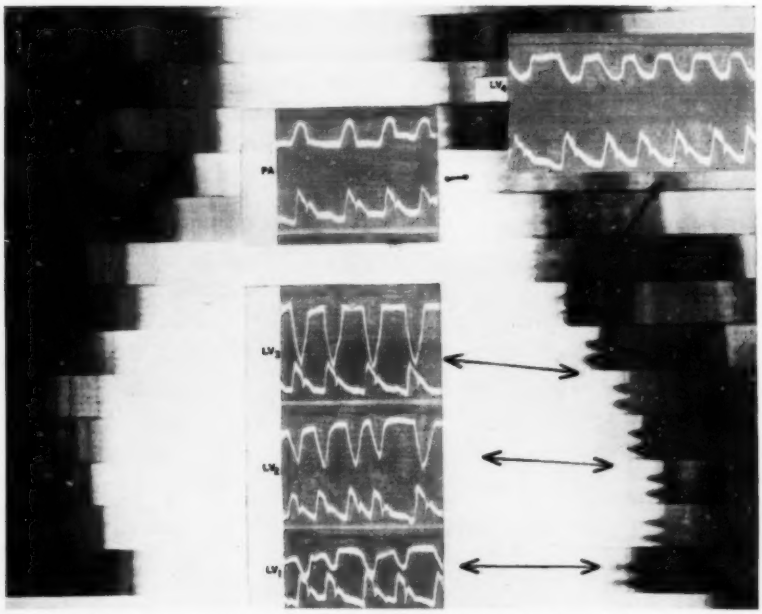

FIG. 5. This patient, case 2 (1), had auricular fibrillation at the time of these pre-operative EKY's and RKY's. The EKY's show, in addition to the characteristic ventricular border pattern, abnormally flat diastolic intervals in the pulmonary artery tracings (PA). There are late systolic plateaus in LV4. The roentgenkymogram, in addition to revealing conspicuous diastolic plateaus, demonstrates, first, the large amplitude of pulsations at the left border in spite of generalized pericardial involvement and secondly, the effect of tachycardia in producing obliteration of the diastolic plateaus. Note the evidence of calcification on the left border.

TABLE I
ELECTROKYMOGRAPHIC FINDINGS

	NUMBER OF STUDIES	PATHOGNOMONIC "FLAT-TOPS AND V'S"	ATYPICAL	NORMAL
Pre-operative studies in constrictive pericarditis	12	11	1	
Post-operative studies in constrictive pericarditis	14	5*		9†
Asymptomatic pericardial calcification	3			3

* All five of these studies were in patients whose manifestations of constrictive pericarditis continued after operation.

† All nine of these studies were in patients who had clinical cures of their constrictive pericarditis following pericardectomy (Figs. 3 and 8).

ventricular silhouette from which recording is made too near one or the other end of the pick-up slit. As the University of Pennsylvania group (14, 15) has

pointed out, in the EKY head of conventional design the sensitivity falls off sharply toward the ends of the slit. If the ventricular border were located near one end of the slit in diastole an artefactual diastolic "flat-top" might result, whereas, if the border were too near an end of the slit toward the end of a systole, a medial, or systolic, plateau might occur.

It is interesting to observe that the "flat-top" is largely wasted time for the heart—cardiac activity is at a standstill. It is clear, therefore, as has been confirmed by study of output after atropine administration (16), that speeding the

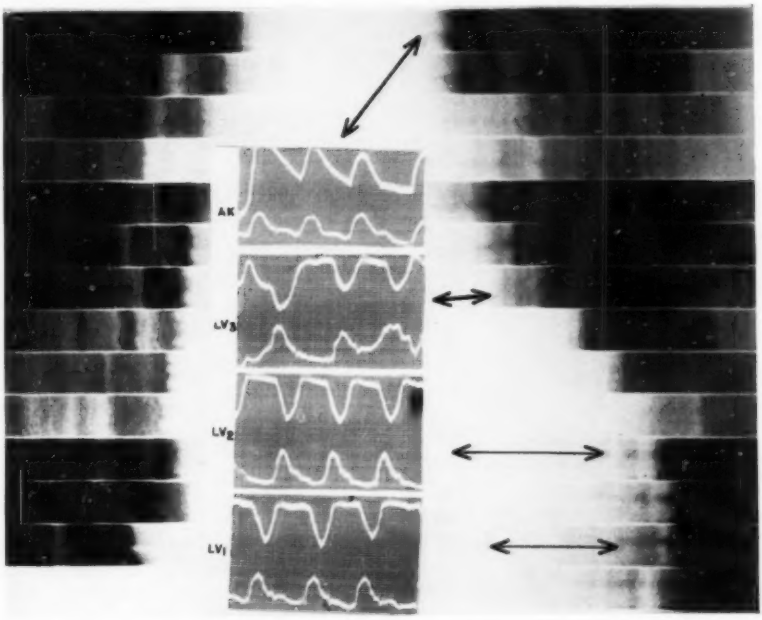

FIG. 6. These kymograms from Case 11 (1) show extensive calcification of the left heart border and the characteristic "flat-top and V" pattern.

constricted heart will improve cardiac output without expense to cardiac filling. In mitral stenosis, on the other hand, cardiac output is likely to drop with acceleration of the heart because of shortening of the left ventricular filling time which may be critical in mitral valve narrowing. Change in cardiac output with atropinization may be a point for differentiation between mitral stenosis and constrictive pericarditis.

The characteristic ventricular motion which is recorded electrokymographically as a "flat-top and V" pattern is occasionally very obvious in fluoroscopy, on physical examination or at operation. Roessler (17) states that occasionally

in some areas the ventricular motion may have "a great amplitude with a rapid diastolic outward movement." He also mentions the important differential point: "It reminds one, at first glance, of that seen . . . in marked bradycardia." Several of the cases in this series, particularly cases 3 and 8, had relative absence of constricting calcification in the region of the cardiac apex with what was in essence a herniation of the ventricle at that site. Fluoroscopically, this area of the ventricle showed movement which was grossly "flat-top and V" in character. The cases in whom this characteristic type of ventricular movement was apparent on physical examination are those in whom part of the left ante-

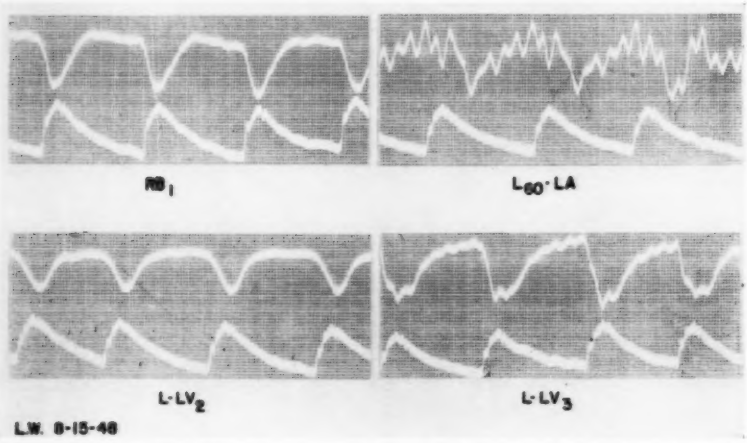

FIG. 7. This patient did not have constrictive pericarditis. He had chronic auricular flutter with complete atrio-ventricular dissociation. Note the auricular flutter waves in L60-LA. The pattern in RB1 and L-LV2 simulates that of constrictive pericarditis as frequently occurs in the presence of bradycardia. The pattern differs from constrictive pericarditis in that first, the filling limb of the "V" is less steep than the ejection limb and secondly, secondary components, especially isometric relaxation are clearly indicated in some tracings (e.g. L-LV3).

rior costal cage had been removed for pericardectomy but the manifestations of constriction continued after operation. Cases 13 and 14 (1) were of this type. In early diastole the ventricle expands rapidly and produces a forceful impact against the hand. Case 20 (1) in contrast to these two cases, for this patient, who has had apparent cure from pericardectomy with normal electrokymograms, has normal cardiac action as seen and felt through a large operative defect in the left anterior chest wall.[2]

[2] Under the term "diastolic heart beat" Wood (18) has recently re-emphasized the diagnostic value of systolic retraction and diastolic lift or impact which is a simple physical expression of the "flat-top and V" pattern of the EKY.

"Flat-top and V" type of movement may even be discernible electrocardiographically! In case 14 (1), V3 was recorded over the center of the chest defect. There was a fairly consistent negative spike occurring soon after the T-wave and due probably to jarring of the electrode by the water-hammer effect at the end of ventricular filling.

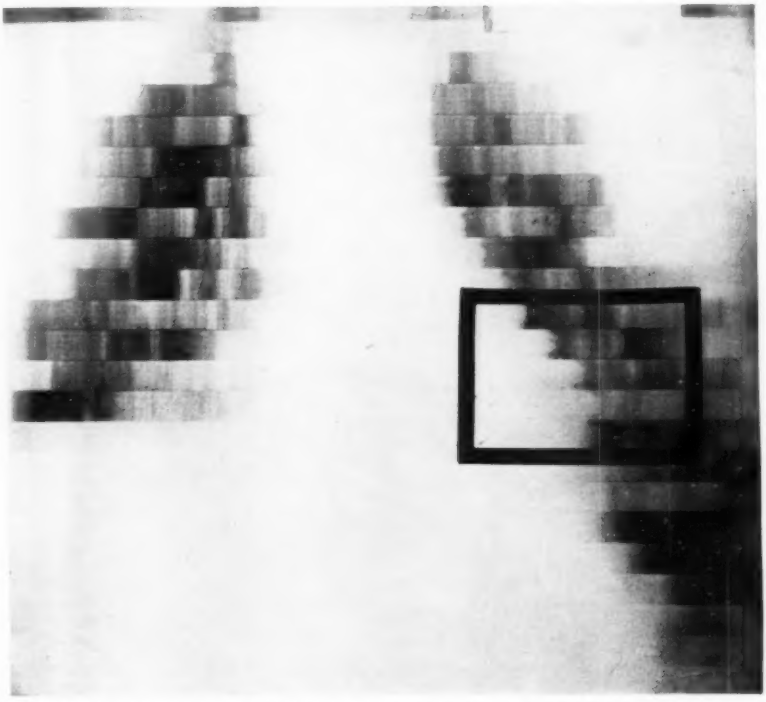

FIG. 8. This patient, case 15 (1), had only roentgenkymograms pre-operatively.

A. The left border shows conspicuous diastolic plateaus. Also demonstrated are the high right diaphragm due to hepatic enlargement and fullness in the region of the superior vena cava.

These studies lead the writer to believe that the electrokymographic pattern described is essentially an all-or-none reaction, i.e., it has no value in localizing constriction as an aid to the surgeon. With the current surgical philosophy that the scar should be removed to as large an extent as possible, information as to location of maximal constriction may be of less importance (19).

All three cases of pericardial calcification without the constrictive syndrome did not show the "flat-top and V" pattern. It is not always easy to identify a case of pericardial calcification as "asymptomatic." One of our patients who

was subsequently so labeled had bouts of left ventricular failure. It was believed that this was due to his hypertension; that constrictive pericarditis was not the cause is probably proved by the absence of the "flat-top and V" pattern in electrokymograms.

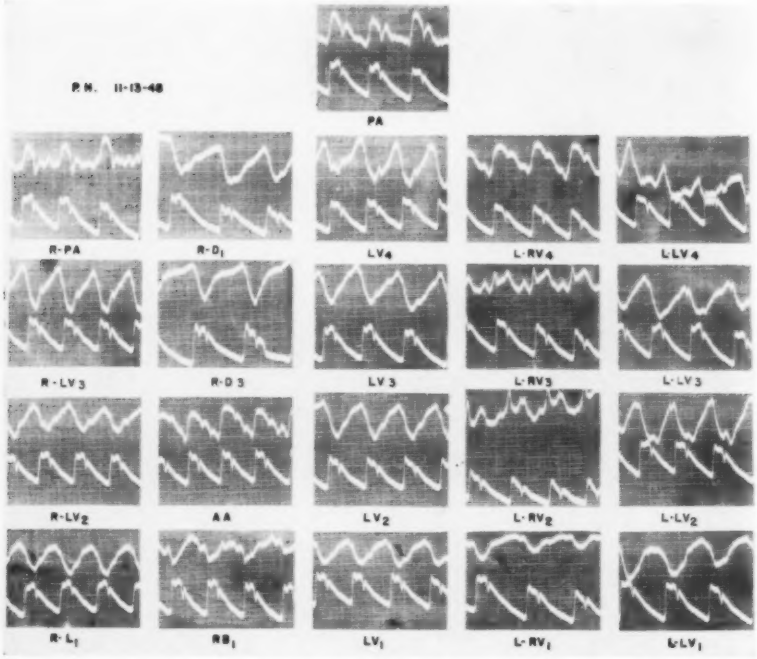

FIG. 8

B. These electrokymograms show return to a normal pattern of ventricular border movement. The patient attained clinical cure.

FINDINGS OF ROENTGENKYMOGRAPHY

As might be anticipated a very close correlation was found between EKY's and RKY's (Figs. 4, 5, 6, 8). Since the electrokymograph as used in these studies provides no means for accurate calibration of border excursion, one must rely on the roentgenkymograms for information as to absolute amplitude of border movement and on the electrokymograms for demonstration of diagnostic changes in the pattern of border movement. However, more often than not the roentgenkymograms also show the "flat-top and V" pattern. Since in electrokymography amplitude of recordings can be controlled, the characteristic pattern may be demonstrated even in areas with little motion by roentgenkymography.

In constrictive pericarditis roentgenkymograms may show normal or increased amplitude of contraction in some or most areas of the ventricular silhouette. It has been held (20) that this increased pulsation is the result of summation of contraction of right and left ventricles. The explanation is probably a simple one: the ventricle contracts with compensatory increase in amplitude in all areas where there is relatively less impediment to motion. Cases 3 and 8 (1) had essentially a herniation of the heart in the region of the cardiac apex where, because of greater mobility, one might anticipate resistance to the development of constriction. Obviously this paradoxically large amplitude of ventricular border excursion may be a source of confusion if the roentgenologist or clinician anticipates diminished excursion as the only kymographic sign of constrictive pericarditis. It is our experience that the cases with areas of increased excursion show the lateral plateaus on RKY and "flat-top and V's" on EKY especially prominently in these same areas. For greatest success in demonstrating the "flat-top and V" pattern by roentgenkymograms, they should be taken in right and left anterior oblique positions as well as in the conventional postero-anterior projection.

SIMULTANEOUS RECORDING OF EKY AND RIGHT HEART PRESSURE CURVES

Figure 9 represents a simultaneous recording of EKY and right heart pressure curves. The ventricular pressure curve shows an artefactual flattening at the peak pressure level. The point of main interest is the timing of the early diastolic "dip" (1) as indicated by comparison with the EKY. The "dip" occurs during the phase of rapid filling of the ventricle.

Superficially the simultaneous EKY and ventricular pressure curves are similar to the tracings of ventricular volume and ventricular pressure recorded by Katz (21) from a model using the turtle heart. These curves were presented as evidence for a suction action of the relaxing ventricle. Cotton (22) pointed out that the presence of a narrowing in the inflow system was necessary for recording the diastolic "dip" from the model. This narrowing prevented instantaneous equilibrium of pressure between the reservoir and the ventricular cavity with a resulting early diastolic "dip." In clinical constrictive pericarditis localized pre-ventricular inflow obstruction is absent (1) in the majority (probably all) of cases. For this reason the analogy to Katz' model is not apparent to the writer.

The right auricular pressure tracing also shows, during the ventricular filling phase, a "dip" which from calibrated recordings has been found to be of roughly the same absolute amplitude as that in the ventricle. This quantitative identity together with the close similarity in the contour of the early diastolic portions of the ventricular and auricular curves may be evidence that the early diastolic "dip" is a bona fide cardiodynamic phenomenon.

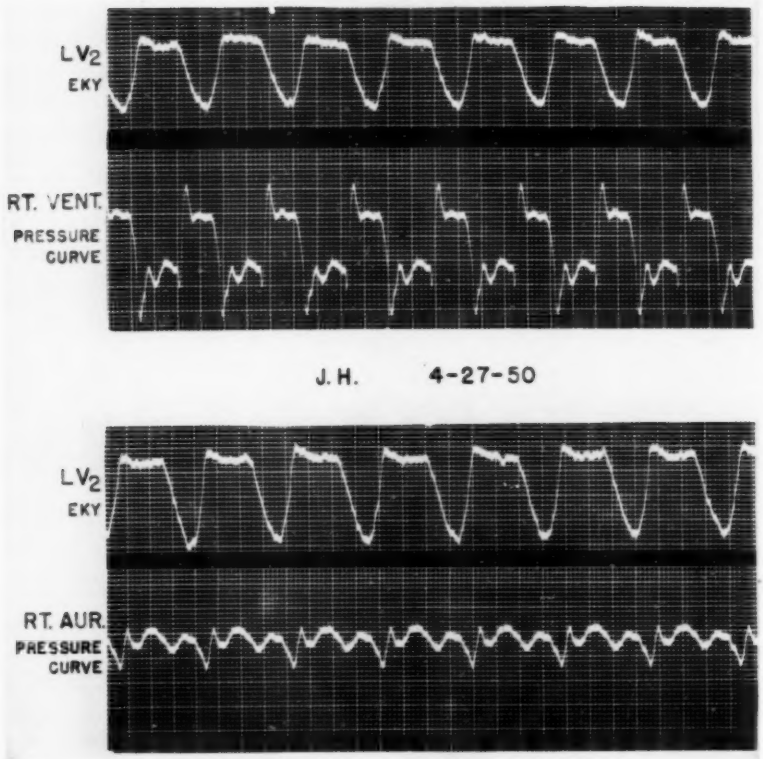

FIG. 9. These recordings of intracardiac pressures and the ventricular EKY were made in patient 13 (1). In the upper tracings the simultaneously recorded right ventricular pressure curve and EKY are presented. There is an artefactual flattening at the systolic peak of the pressure curve. The early diastolic "dip" and diastolic plateau are well demonstrated. The early diastolic "dip" is synchronous with the rapid filling limb of the electrokymogram.

The right auricular pressure curve shows the same wave form during rapid ventricular filling and immediately thereafter as does the right ventricular pressure curve. This may be evidence that the early diastolic "dip" is bona fide.

THE PROTODIASTOLIC SOUND OF CONSTRICTIVE PERICARDITIS

Clinical aspects of this finding have been presented in an accompanying article (1). Figure 10 is representative of the time relationships when heart sounds and EKY are recorded simultaneously. The protodiastolic sound is synchronous with the end of rapid ventricular filling and with the abrupt halt in filling which occurs at the beginning of the diastolic plateau. Probably the sound is, at least in part, a water-hammer phenomenon.

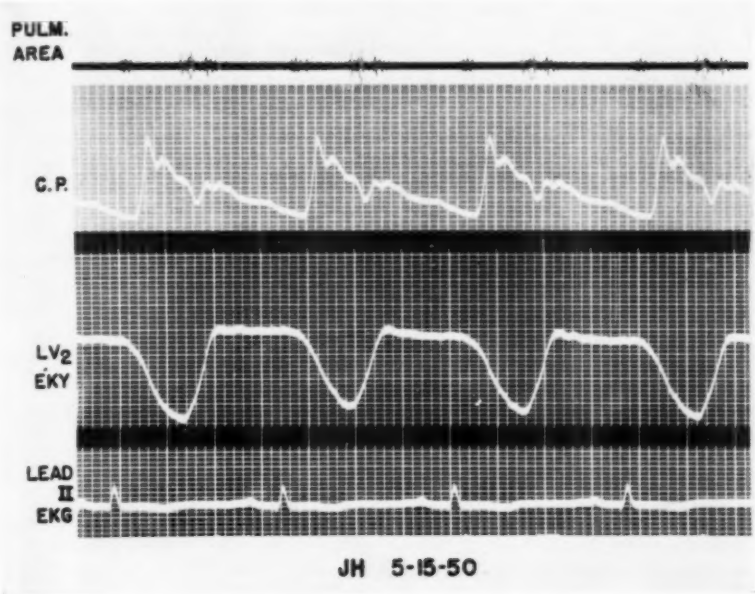

FIG. 10. This patient, case 13 (1), has a split second sound but in addition a prominent protodiastolic sound. The protodiastolic sound occurs toward the end of rapid ventricular filling as demonstrated by the EKY. Carotid pulse and EKG are also recorded.

GENERAL COMMENTS

That the fundamental physiologic defect in constrictive pericarditis is an impediment to diastolic filling of the ventricle is quite generally accepted. The observations reported here lend further support to this thesis. The several phenomena observed in this condition are all based on the filling defect:

1. The "flat-top and V" pattern of the EKY.
2. The adventitious protodiastolic sound.
3. The early diastolic "dip" and diastolic plateau of the ventricular pressure curves (1).
4. The large diastolic excursions of the ballistocardiogram (23).
5. The "diastolic heart beat" of Wood (18).

That many cases of constrictive pericarditis have some degree of cardiac enlargement (24) is not inconsistent with the view that the predominant defect is one of ventricular filling. However, undoubtedly, there is, in such cases, a defect of ventricular emptying as well. That such is the case appears to be indicated by the residual ventricular volume studies of Bing (25).

SUMMARY AND CONCLUSIONS

1. The electrokymographic pattern of "flat-tops and V's" is highly diagnostic of chronic constrictive pericarditis.

2. At present one must rely on roentgenkymography for information as to absolute amplitude of ventricular border movement and on electrokymography for details of the pattern of that movement. However, more often than not, roentgenkymograms also show the "flat-top and V" pattern.

3. Electrokymograms are a valuable index of results of pericardectomy.

4. Normal patterns of ventricular border movement were found electrokymographically and roentgenkymographically in three cases of clinically asymptomatic pericardial calcification.

5. The early diastolic "dip" of the right ventricular pressure curve occurs during the rapid filling phase.

6. The protodiastolic sound of constrictive pericarditis is produced by rapid ventricular filling and abrupt halt in filling.

ACKNOWLEDGEMENTS

The writer is greatly endebted to Dr. Luther L. Terry, who stimulated his interest in electrokymography. Dr. Richard G. Oakley assisted in the early stages of the study. Miss Clara King gave valuable technical assistance.

ADDENDUM

Since this manuscript was prepared two more cases of constrictive pericarditis have been studied and submitted to decortication with success. Both showed the kymographic pattern described here. Awareness of the characteristic pattern as a result of the detailed electrokymographic analyses makes roentgenkymography more informative and electrokymography less essential to the diagnosis.

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THE BALLISTOCARDIOGRAM IN CONSTRICTIVE PERICARDITIS BEFORE AND AFTER PERICARDIECTOMY

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INTRODUCTION

The interest which has been renewed in chronic constrictive pericarditis in recent years is attributable to the gratifying results achieved through the surgical removal of the constricting pericardial shell (1–5) and to the development of newer diagnostic methods which have allowed the diagnosis to be made with a greater degree of certainty. Detailed analysis of the motion of the heart borders has been made possible by the development of the electrokymograph (6) and characteristic curves have been described in constrictive pericarditis (7–9). Cardiac catheterization has allowed careful study of the alteration in circulatory dynamics occurring in patients with this condition and right auricular and right ventricular pressure curves considered characteristic have been described (10).

The ballistocardiograph is an instrument designed to record movements of the human body caused by the flow of blood within the cardiovascular system. Since the pioneer work of Starr (11) it has been used as a method for estimating cardiac output in normal individuals under varying physiological conditions which produce quantitative changes in the record and has been applied to the study of various types of cardiovascular abnormalities in which qualitative alteration of the record is frequently found. Since the ballistocardiograph is sensitive to changes in the velocity of blood flow it is not surprising that the largest deflections occur during systole when the heart ejects blood at high velocity into the great vessels. In the normal individual ventricular systole produces a characteristic pattern or wave-form which varies but little from person to person. In contrast, the waves produced during diastole are much smaller and vary considerably from one individual to another. Due, in part, to the after-oscillations of the body following the large systolic vibrations, these diastolic waves are usually largest in early diastole and tend to die out before the next systole.

Standard ballistocardiograph beds are designed in such a manner as to re-

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cord only those body movements which are parallel to the long axis of the body. In a previous report (12) a method (vector ballistocardiography) was described which permits body movements to be recorded in all three directions, i.e. head-foot, side-to-side and front-to-back; recent work suggests that important information may be present in the vector records but partially or completely absent in the head-foot record.

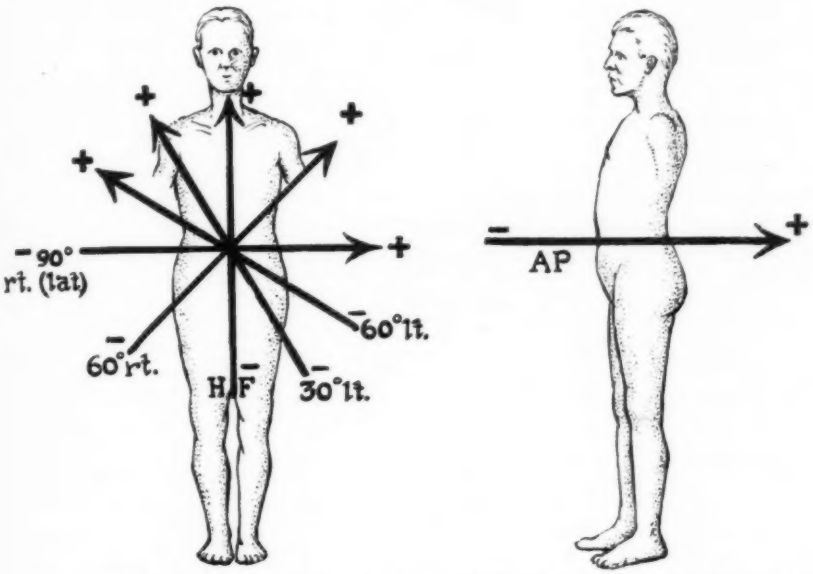

FIG. 1. This diagram illustrates the various recording axes used in taking ballistocardiographic vector records with the turntable. The direction of each arrow indicates the direction in which the ballistocardiograph bed is free to move and record. A movement toward the head of the arrow produces an upward or positive deflection on the record.

The present study was undertaken to delineate the changes in the ballistocardiograms of patients with constrictive pericarditis and to relate the ballistocardiographic pattern to the results of other diagnostic methods and to the known circulatory alterations produced by this condition. In addition, changes in the ballistocardiogram following pericardiectomy were studied and were correlated with the clinical results of operation.

METHOD AND MATERIALS

A standard high-frequency ballistocardiograph bed was used in this study; a light wooden turntable was placed on its flat top and could be rotated about a central pivot. This allowed records to be taken at any angle in the frontal plane and by turning the subject on his right side with the bed in the lateral position records could be made in the A-P direction. Figure 1

shows the different recording axes employed. The arrow in each case indicates the direction in which the ballistocardiograph bed is free to move and record. Thus at 60° rt. the bed is free to move only in the direction indicated by the arrow. A movement toward the head of the arrow produces an upward or positive deflection on the record while one toward the tail of the arrow produces a downward or negative deflection. In the 60° rt. position the turntable has been rotated (counter-clockwise viewed from above) 60° away from the head-foot axis; the term "rt." refers to the side of the body which faces the foot end of the ballistocardiograph bed. In the 60° lt. position the left side of the body faces the foot of the ballistocardiograph bed. In the 90° rt. (or lateral position) side-to-side movements are recorded and in the A-P position front-to-back movements are recorded. Normal individuals have similar vector records (see Fig. 3, Normal Subject). In the 60° rt. position, the I, J and K waves are about one half the size of these waves in the head-foot record. In the 90° position small but distinct I, J and K waves are usually seen; diastolic waves are small or absent here. Records are taken routinely in the head-foot (H-F), 30° lt. (or 60° lt.), 60° rt., 90° rt. and A-P positions. An electrocardiogram (lead 2) served as a cardiac time reference. Respiration was indicated by means of a belt-pneumograph. Heart sounds were recorded with a Cambridge microphone. Apex cardiograms and jugular pulse tracings were taken with a Sanborn pulse pick-up. Heavy time lines on the records are at intervals of 0.1 sec. Amplitude of the ballistocardiograph was calibrated so that 280 gms. produced a deflection of 1 cm.; this calibration is indicated on a record in each figure by a vertical line bracketed at either end by a short horizontal line.

A total of ten patients were studied and these may be placed in three separate groups: A) 3 patients studied both before and after pericardiectomy, B) 2 studied pre-operatively only and C) 5 studied post-operatively only. The diagnosis of constrictive pericarditis was confirmed in 9 of the 10 at operation; in the remaining case diagnostic studies indicated definite, though mild, constrictive pericarditis. All of these patients have been extensively studied and the clinical aspects of the cases as well as the results of other diagnostic methods are reported elsewhere (9, 13). All of them had electrokymograms (referred to hereafter as EKYs) and/or roentgenkymograms (referred to hereafter as RKYs) before and after operation. The characteristic EKY and RKY finding in constrictive pericarditis will be described as the "flat-top and V" pattern (9). Most of the patients were subjected to cardiac catheterization; the pressure curve from the right ventricle in this condition will be termed the "early diastolic dip and plateau" pattern while that from the right auricle will be called the "M-shaped" pattern (10).

RESULTS

A. Cases Studied Before and After Pericardiectomy:

Case 1 (C. M.)—Figures 2 and 3 show the ballistocardiograms on this 62 year old man, who had the typical clinical findings of constrictive pericarditis including a protodiastolic sound. RKYs revealed decreased ventricular pulsations with diastolic plateaus and EKYs showed the typical "flat-top and V" pattern. Cardiac catheterization revealed a typical right ventricular "early diastolic dip and plateau" pressure curve and a characteristic "M-shaped" right auricular pressure curve.

The pre-operative ballistocardiogram was abnormal. In the head-foot record during normal breathing (Fig. 2, Pre-op) form varied considerably during the respiratory cycle. During expiration there were waves which arose in diastole and appeared to "ride into" the systolic waves, distorting their form. In the H-F record during held respiration (Fig. 3, Pre-op) a small insignificant late diastolic wave was seen. However, in the vector records there were

diastolic waves of great magnitude which dominated the tracings; these waves began in early diastole, lasted throughout diastole and seemed to continue into early systole.

On 7/28/50 a pericardiectomy was performed by Dr. Alfred Blalock; almost complete resection of the thick, adherent pericardial scar was possible. Following operation there was striking improvement in symptoms and signs. Ten days after operation a second ballisto-

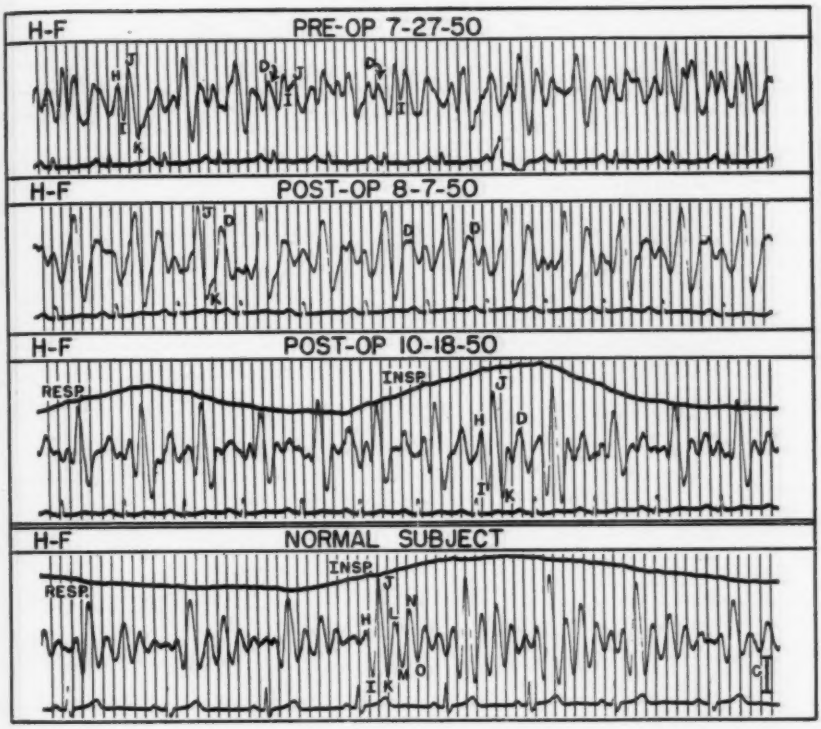

FIG. 2. Case #1 (C. M.) Constrictive Pericarditis. Records taken during normal breathing. Record from a normal subject shown at bottom; the calibration (1 cm. = 280 gms.) indicated by vertical line at extreme right of this record (C) applies to other tracings also. D refers to diastolic waves in this and in all subsequent figures. Heavy time lines are 0.1 sec. "Resp." refers to respiration; inspiration upward. Pericardiectomy on 7/28/50. See text for description.

cardiogram (8/7/50) showed considerable improvement but the I wave was broadened and distorted and the I-J segment was slurred; whether this was due to "ride-in" from late diastolic waves or to true early systolic abnormality was not clear. However, the large mid-diastolic waves, so prominent a feature of the previous vector records, had practically disappeared. It should be noted that although the head-foot I wave was slurred and distorted, in the 60° rt., 90° rt. and A-P positions it was clear-cut and sharp. An EKY at this time revealed that the "flat-top and V" pattern had disappeared.

A third ballistocardiogram was made 2½ months after operation (10/18/50). There was further improvement in form and the head-foot record during normal breathing was practically normal. Complexes during expiration and during held respiration showed small short I waves and deep K waves but the gross distortion of the I wave seen in the previous record had disappeared. An RKY at this time showed excellent pulsations of the left ventricle except for a portion of the apex which appeared to be restricted by a fibrous band. Para-

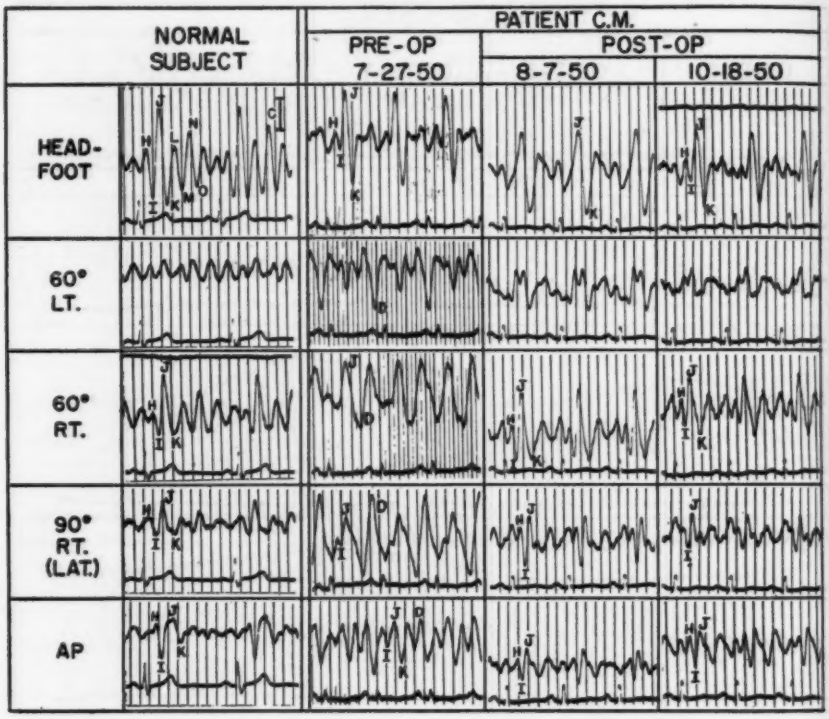

FIG. 3. Case #1 (C. M.) same as in Figure 2. Records taken during held respiration. Records from normal subject in column on left; calibration on Head-Foot strip in this column applies to all tracings. See text for description.

doxical pulse and the protodiastolic sound had disappeared; venous pressure was normal and exercise tolerance was quite good.

Case 2 (L. N.)—The ballistocardiograms on this 17 year old boy are shown in Figures 4 and 5. Clinical findings were typical and included an apical protodiastolic sound. An RKY showed ventricular pulsations which were "mere vibrations." An EKY was not entirely satisfactory because the motion of the left border was not well seen; there were no typical "flat-tops and Vs" but there was thought to be late systolic expansion of a portion of the left ventricle.

The pre-operative ballistocardiogram was grossly abnormal (Figs. 4 and 5). The systolic complexes were difficult to identify in the head-foot records. There were moderately large

waves occupying most of diastole and in some instances appeared to continue into systole. A deep footward wave in early systole, shortly after the R wave of the electrocardiogram, was a consistent feature of the record. The diastolic waves were more striking in the vector records (Fig. 5, Pre-op) where they equaled or exceeded the systolic waves.

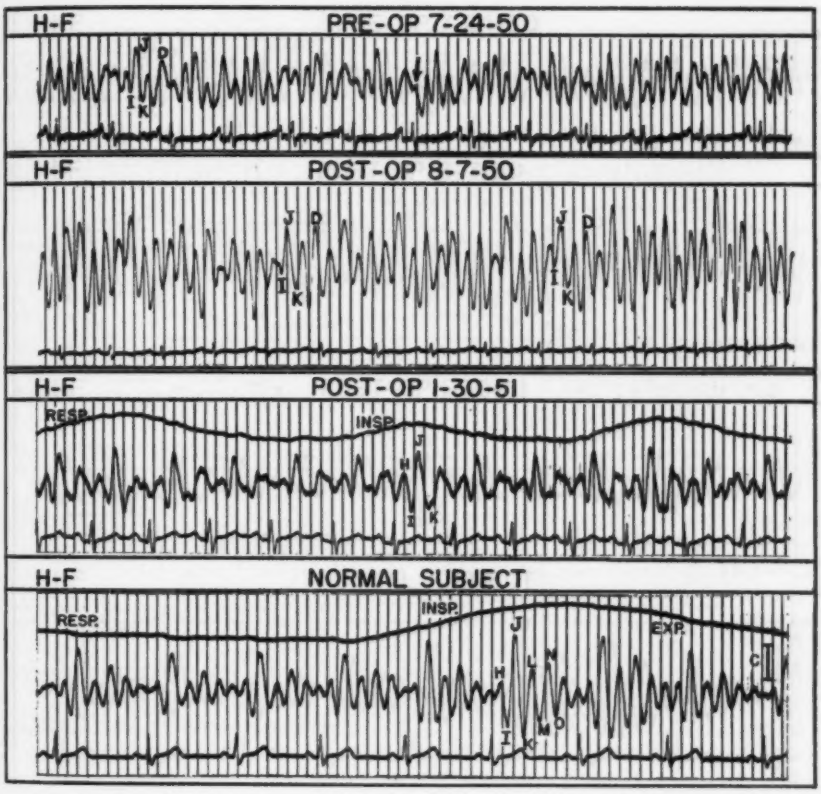

FIG. 4. Case #2 (L. N.) Constrictive Pericarditis. Records taken during normal breathing. Normal subject at bottom; calibration on this strip also applies to other tracings. Arrow indicates deep footward wave occupying early systole. Pericardiectomy on 7/25/50. See text for description.

On 7/25/50 a pericardiectomy was performed by Dr. Alfred Blalock and most of the scar was removed from both ventricles and both auricles. Following operation there was remarkable clinical improvement with a gradual drop in venous pressure to normal, disappearance of ascites, hepatomegaly, paradoxical pulse and protodiastolic sound.

The ballistocardiogram recorded 13 days after operation (Figs. 4 and 5, Post-op., 8/7/50) showed striking changes. The head-foot record showed almost continuous oscillations and the diastolic waves were more prominent than in the pre-operative record. The vector records showed that the diastolic waves were more prominent and of a different character,

being almost entirely upward at 60° rt. and 90° rt. "Ride-in" by the diastolic waves into systole was clearly demonstrated. Of much interest were the results of an EKY and RKY done 4 days after the ballistocardiogram. The RKY showed that ventricular pulsations were of good amplitude with an apparently normal pattern. The EKY studies showed no "flat-top and V" pattern.

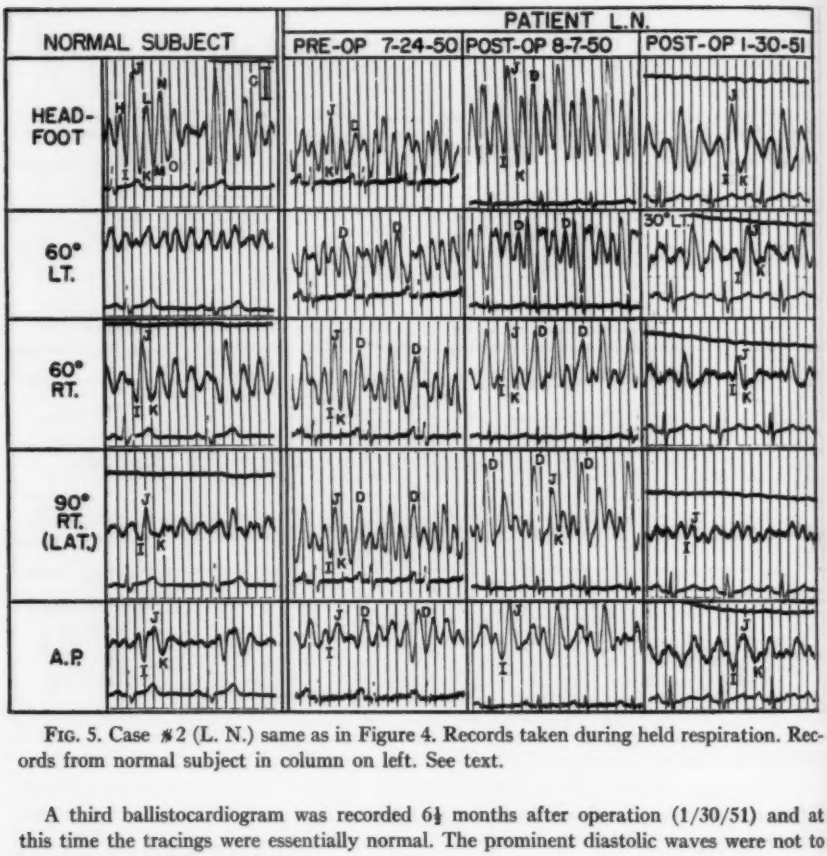

FIG. 5. Case #2 (L. N.) same as in Figure 4. Records taken during held respiration. Records from normal subject in column on left. See text.

A third ballistocardiogram was recorded 6½ months after operation (1/30/51) and at this time the tracings were essentially normal. The prominent diastolic waves were not to be seen in any of the tracings.

All of the clinical signs of constrictive pericarditis have disappeared in this patient and he is now considered a clinical cure.

Case 3 (L. W.)—This 49 year old man had history and physical findings which were typical of constrictive pericarditis. There was no protodiastolic sound although one was described in another hospital earlier. An RKY showed little or no ventricular motion in most areas but in the right anterior oblique view pulsations with a "flat-top and V" pattern were seen. An EKY showed the typical "flat-top and V" pattern of ventricular motion.

The pre-operative head-foot ballistocardiogram was essentially normal. However, large mid- or late diastolic waves appeared occasionally and these seemed to occur only near the

end of inspiration or the beginning of expiration; small waves appeared at the same point in diastole in other complexes but were generally insignificant. The vector records showed diastolic waves of moderate size. In most instances these appeared as tall "L waves" early in diastole. Although diastolic "ride-in" into the systolic complexes was not obvious, it was suspected in the 60° rt. record where the I appeared to begin early (at the time of the R wave) and in the 90° rt. record where there was a "doubled I wave."

On 7/19/50 pericardiectomy was performed by Drs. Richard Kieffer and Alfred Blalock. Complete removal of the thick fibrous scar was carried out except for a small area over the anterior surface of the left ventricle. The clinical response was satisfactory and within a week venous pressure had dropped to upper limits of normal. Nine weeks after operation he was symptom-free and had no venous distension or edema. However, a protodiastolic sound was heard at this time.

At this time a post-operative ballistocardiogram was considerably more abnormal than the pre-operative record had been. The head-foot record during normal breathing showed mid-diastolic waves of considerable amplitude in most of the cardiac cycles. In the vector records the mid-diastolic waves were clear-cut and there was definite distortion of the I waves by "ride-in" from diastolic deflections. An RKY 2 weeks prior to this ballistocardiogram showed normal amplitude and pattern of ventricular motion and an EKY showed suggestive "flat-tops and Vs" from the lower left ventricle but nowhere else. It has not been possible to secure a late follow-up ballistocardiogram on this patient who was definitely benefitted by pericardiectomy.

B. Cases Studied Pre-Operatively Only:

Case 4 (W. M.)—This 57 year old man had typical physical findings of constrictive pericarditis; there was also a protodiastolic sound and systolic precordial retraction. His case was complicated somewhat by a history of hypertension and of anterior chest pain produced by exercise and relieved by rest. Pre-operative roentgenographic findings included a normal sized heart with pericardial calcification about both ventricles. RKYs showed decreased cardiac pulsations, "flat-tops and Vs" from both ventricles and systolic plateaus from the upper left ventricle. Systolic expansion of the right ventricle, systolic plateaus from the left ventricle as well as the typical "flat-top and V" pattern were demonstrated in the EKYs.

The ballistocardiogram (Fig. 6A) was abnormal. The head-foot record showed small mid- and late diastolic waves which appeared to "ride into" and distort the systolic complex. The vector records, especially that at 60° rt., showed large waves beginning early in diastole and running up to, and possibly into, systole. At operation the heart was found to be encased in a "dense shell of bone." Before decortication could be attempted the blood pressure dropped and heart action ceased; efforts at resuscitation were unavailing. This death was the only one among the cases reported here.

Case 5 (N. D.)—In Figure 6B is shown the ballistocardiogram on this 35 year old man who has had relatively mild symptoms. Physical findings included slight venous distension with a prominent jugular pulse, a paradoxical pulse and hepatomegaly but no protodiastolic sound was heard and there was no ascites or edema. An RKY revealed decreased pulsations of some portions of the ventricles with suggestive diastolic plateaus. The first electrokymographic study showed no definite plateaus from the ventricles while a repeat examination one year later did show left ventricular diastolic plateaus. Two cardiac catheterizations were carried out. The first showed a low cardiac output, elevated right auricular pressure, elevated right ventricular end-diastolic pressure and a right ventricular pressure curve with an early diastolic dip. Six months later cardiac output had risen to normal and right ventricu-

lar end-diastolic pressure was lower but the right auricular pressure was still elevated and the right ventricular pressure curve had the same contour.

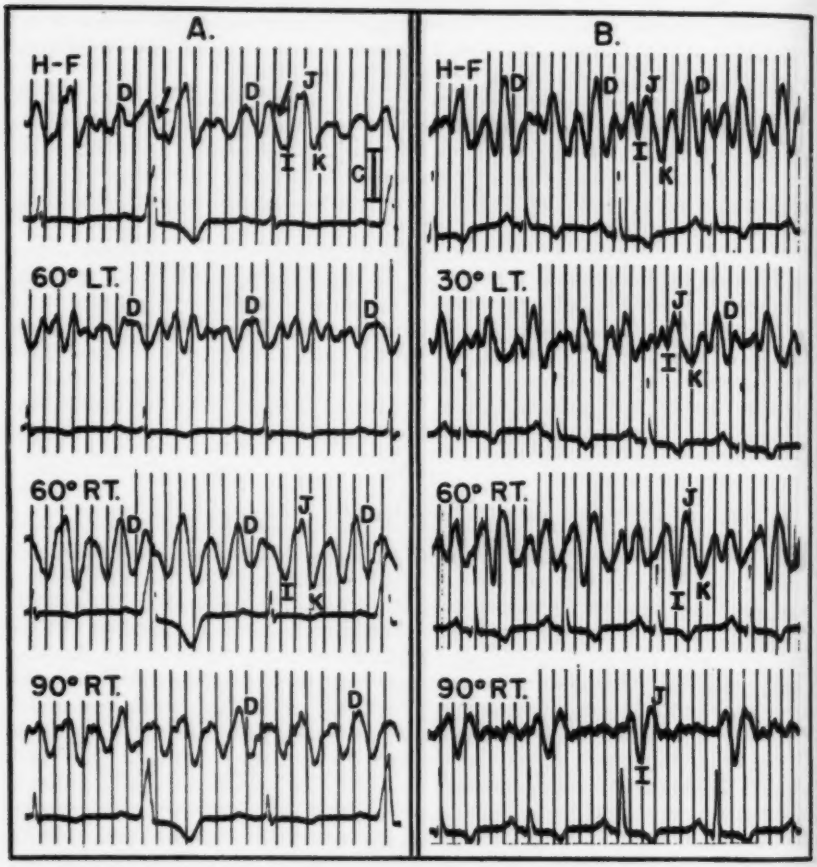

FIG. 6A. Case #4 (W. M.) Constrictive Pericarditis, Pre-Operative, held respiration. Arrows indicate distortion to initial portion of systolic complex. See text.

FIG. 6B. Case #5 (N. D.) Constrictive Pericarditis, Pre-Operative, held respiration. Note that the diastolic waves are larger than the systolic in the H-F (Head-Foot) record, but are absent at 90° rt. (Lateral). See text.

The ballistocardiogram shown in Figure 6B was taken during suspended respiration. The head-foot record showed small systolic complexes and large waves occupying mid-diastole; these waves resemble the normal systolic complex. Smaller diastolic waves were present in the 30° lt. and 60° rt. records but none were present in the 90° rt. position. These records are in contrast to those from the other cases in whom diastolic waves were usually greater in the vector records. Furthermore, during normal breathing, the head-foot diastolic waves

in this patient varied considerably during the respiratory cycle and practically disappeared during inspiration. There was no "diastolic ride-in" into systole in these records.

This patient has not been subjected to pericardiectomy because of the mildness of his symptoms. He has continued to do well and when last seen in July 1951 stated that he noted dyspnea only on unusual exertion.

C. Cases Studied Post-Operatively Only:

Case 6 (W. B.)—This 17 year old male had clinical findings consistent with marked constrictive pericarditis. RKY and EKY examinations revealed diminution in amplitude of the ventricular pulsations with the "flat-top and V" pattern. The pressure curve from the right ventricle showed the "early diastolic dip" and that from the right auricle showed the "M-shaped" contour. At operation it was possible to dissect the dense adherent pericardium from the entire heart and the vena cavae. Pericardiectomy produced an excellent clinical result with a fairly rapid disappearance of abnormal findings. One month after operation an RKY showed good pulsations of the entire heart. A ballistocardiogram at this time showed an almost normal record in the head-foot position but there was evidence of late diastolic "ride-in" producing a footward deflection early in systole before the I wave. This was evident in the vector records which showed, in addition, distinct and moderately large mid-diastolic waves in the 60° rt. and 90° rt. records. Three and one-half months later electrokymographic tracings were entirely normal. A ballistocardiogram at this time was essentially normal. The head-foot record no longer showed late diastolic "ride-in" and while mid-diastolic waves were still present in the 60° rt. record they were small and insignificant.

When last seen in June 1951 this patient was symptom-free and showed no abnormal physical findings. He is considered a clinical cure.

Case 7 (R. McA.)—This 28 year old male was found to have constrictive pericarditis with extensive calcification; the heart was enlarged and auricular fibrillation was present. An RKY showed ample pulsation of the left ventricle but no movement of the right auricle or ventricle. The "flat-top and V" pattern was seen and its presence was confirmed by electrokymography. The right ventricular and right auricular pressures were elevated and the right ventricular pressure curve showed the "early diastolic dip." At operation the adherent pericardium was removed from the entire heart except for a small plaque over the anterior descending coronary artery. Clinical improvement was remarkable and during the next few months all of the abnormal physical findings (except auricular fibrillation) gradually disappeared.

Two years after operation a ballistocardiogram was recorded. The presence of auricular fibrillation with a ventricular rate of 92 made interpretation difficult but the head-foot tracing was almost normal although some of the I waves were slurred and distorted. This was found to occur only in those complexes preceded by a short diastole. No mid-diastolic waves of any significance were present either in the head-foot or the vector records. Previously EKYs had been recorded on 3 different days. The first two sets of tracings revealed auricular fibrillation and a persistence of the "flat-top and V" pattern while the third set failed to show this pattern although the tracings were considered abnormal.

When last seen in July 1951, 16 months after operation, patient was doing remarkably well and was able to perform heavy labor without dyspnea or edema.

Case 8 (E. C. P.)—Figure 7 shows the ballistocardiograms from this 56 year old man who was operated on by Dr. Alfred Blalock in 1946. Pre-operative RKYs showed pulsations of the left ventricle to be of fair amplitude but there were diastolic plateaus. At operation the adherent pericardium was removed from the anterior surface of the heart only. Following operation the patient made a complete clinical recovery and in the 5 years which have

transpired he has been symptom-free and able to lead a normal life. Since operation several RKYs and EKYs have revealed ventricular pulsations of normal amplitude and contour.

Ballistocardiograms recorded on 7/9/51 are shown in Figure 7. The head-foot record during normal breathing (A) was abnormal and showed distortion of the early portion of the systolic complex. Beginning at the peak of the R wave there was a deep sharp footward deflection, early in systole, which varied with respiration and was largest during inspiration. During held respiration (B) this footward wave and the succeeding headward wave dominated the systolic complex, almost obliterating the J wave. Figure 7C shows the apex cardiogram, ballistocardiogram, electrocardiogram (lead 2) and phonocardiogram recorded si-

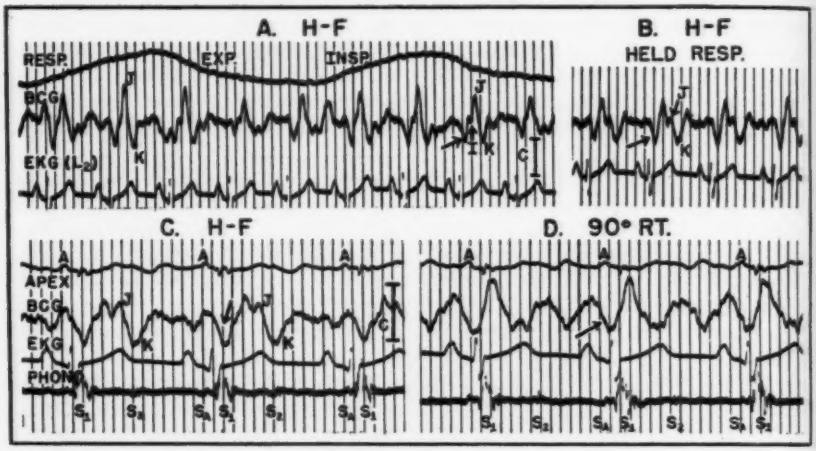

FIG. 7. Case #8 (E. C. P.) Constrictive Pericarditis, 5 Years Post-Operative. A. Head-Foot during normal breathing. Note distortion of early portion of systolic complex; no remarkable mid-diastolic waves present. Calibration on this record also applies to B. B. Head-Foot during held respiration. Early systolic deflections dominate normal systolic complex. C. Head-Foot BCG during held respiration with apex cardiogram, EKG and phonocardiogram. "A" refers to auricular wave (in apex tracing) and "Sa" refers to auricular sound. Note that deep early systolic wave (arrow) appears to begin in late diastole. Calibration and labels also apply to D. D. 90° rt. (Lateral) BCG during held respiration. See text.

multaneously at twice the usual paper speed. The abnormal early systolic wave appears to begin in presystole after the P wave of the electrocardiogram. The apex tracing shows a distinct auricular impulse which begins about the same time as the ballistic wave; apex cardiograms taken with higher amplification show this more clearly. There is a distinct auricular sound in the phonocardiogram. In the 90° rt. record (Fig. 7D) there is a well-defined negative deflection at the time of the R wave followed by a large positive wave in early systole; the beginning of the diastolic wave is not clear in this tracing.

Case 9 (J. H.)—This 26 year old male was first seen here in 1946 with the classical signs of constrictive pericarditis. There was extensive calcification of the pericardium. RKYs showed that pulsations of the right heart border were diminished while those of the left border were large and of the "flat-top and V" type. He has undergone three pericardiectomies, the last in September 1950. There was little change in his clinical state following the

first two operations (in 1947) but there has been some improvement since the last. He has had repeated RKYs and EKYs all of which showed the "flat-top and V" pattern. Right auric-

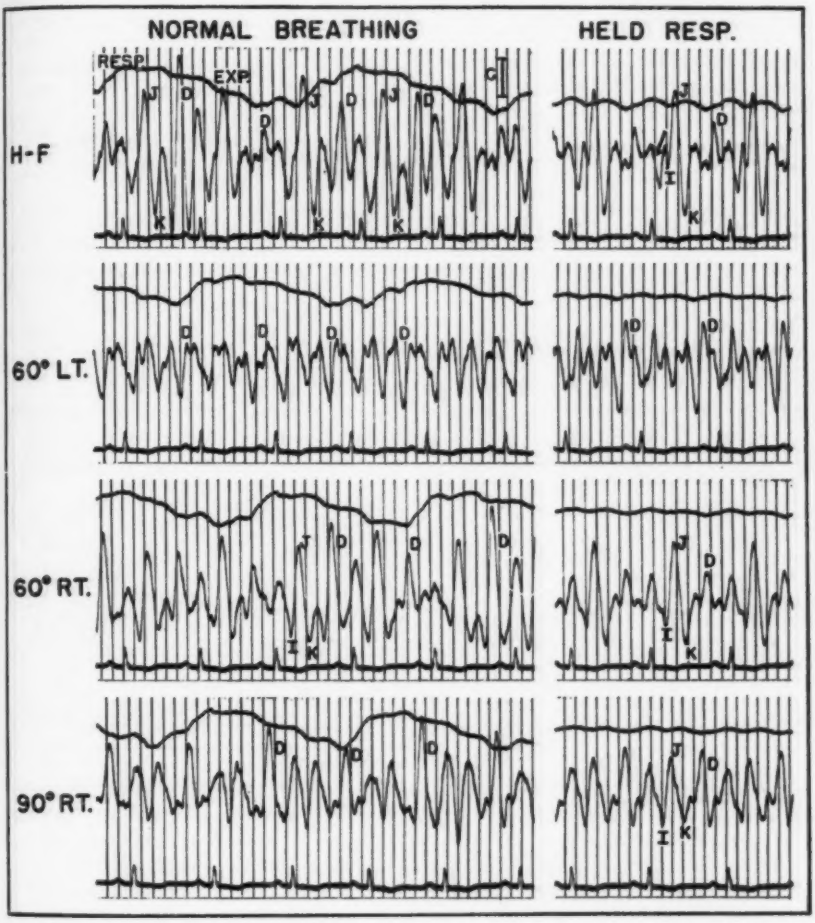

FIG. 8. Case #9 (J. H.) Constrictive Pericarditis, Post-Operative. Large mid-diastolic waves vary with respiration and almost disappear during held respiration in the H-F and 60° rt. records. Note deep early systolic deflection (arrow) in H-F record on right. Calibration applies to all tracings. See text.

ular pressure was elevated and the "M-shaped" curve was present. Right ventricular end-diastolic pressure was elevated and the tracing showed an early diastolic dip.

Ballistocardiograms taken prior to the last pericardiectomy (Fig. 8) were grossly abnormal and showed huge mid-diastolic deflections (up to 4.5 cm. in height) which often exceeded the systolic waves in amplitude and distorted their form; these were present in the head-

foot as well as in the vector records. They were markedly influenced by the phase of respiration and in the head-foot and 60° rt. positions almost disappeared during suspended respiration. Since the last operation, however, there has been gradual improvement in the records although they are still abnormal. Amplitude of the systolic waves has increased and that

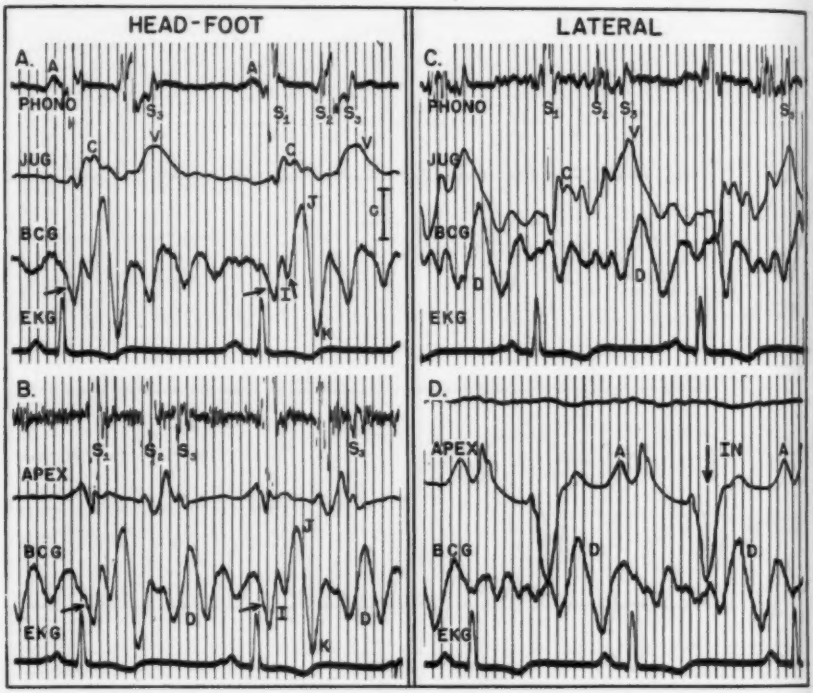

FIG. 9. Case #9 (J. H.) same as in Figure 8. A and B are H-F BCG records, C and D are lateral BCG records. In the phonocardiograms, "A" indicates an auricular deflection, "S_3" the protodiastolic sound. In the apex cardiograms a deflection downward indicates retraction (in), upward expansion (out); "A" indicates auricular precordial thrust. Note the deep, abnormal early systolic ballistic waves in A and B. See text for description.

of the diastolic waves has decreased. The latter are now much less prominent in the head-foot record than in the 90° rt. record.

The ballistocardiograms shown in Figure 9 are the most recent (May 1951) and were chosen in order to illustrate several interesting features. As a result of the three pericardiectomies there is a large defect of the bony cage in the precordial area through which the heart can be seen and felt to pulsate vigorously. In Figures 9A and B the ballistocardiograms were taken in the head-foot position while those in C and D were taken in the lateral position. In Figure 9A the ballistocardiogram shows clearly a large early systolic footward deflection partially cancelling the I wave which appears on the ascending limb of the J wave. The mid-diastolic wave in this record is insignificant. The phonocardiogram recorded through the

chest defect just inside the apex has a peculiar appearance because of the alteration in sound transmission in this area; the curve consists mainly of low-frequency "displacement" components. Well marked auricular waves precede the 1st sound and begin about 0.09 sec. after the beginning of the P wave; no auricular waves appear in the jugular pulse at this time, however. The 2nd heart sound is followed shortly by a protodiastolic sound of low frequency. The beginning of this 3rd sound coincides with the downstroke of the jugular "v" wave, allowing for transmission time to the jugular vein (Figs. 9A and C). Furthermore, these two events coincide in time with the beginning of the ballistic mid-diastolic wave (seen in

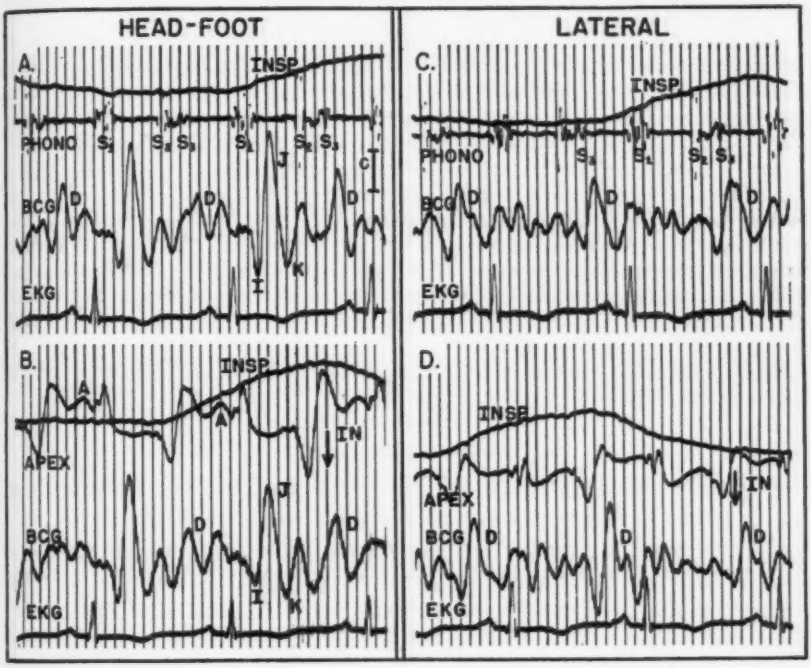

FIG. 10. Case #10 (G. V. S.) A and B are H-F BCG records, C and D are lateral records. Labels same as in Figure 10. See text for description.

Figs. 9B, C and D). The apex tracing shown in Figure 9B was actually taken near the anterior axillary line while the phonocardiogram was taken to the right of the lower sternum, both outside of the chest defect. The apex cardiogram shows a well marked auricular impulse and a sharp protodiastolic apical thrust. In Figure 9D the apex cardiogram, taken over the chest defect, shows a well defined auricular thrust and a deep early diastolic retraction followed by a steep precordial expansion ending in an outward thrust and a plateau. It should be noted that the mid-diastolic ballistic waves begin at the nadir of this precordial impulse. Simultaneous electrokymograms and ballistocardiograms (electromagnetic) on this patient have shown that these ballistic waves begin during the first half of the filling limb of the ventricular electrokymogram and at the time of the sharp negative wave in the

auricular pressure tracing. These findings suggest that the ballistic waves originate early in diastole during the initial period of ventricular filling.

Case 10 (G. V. S.)—This 22 year old female is similar in many respects to the preceding patient. She has had 3 pericardiectomies, the first in 1943 and the last in May 1951. EKYs have continued to show the "flat-top and V" pattern, including those following her last operation. Since this last operation she had shown improvement but it is still too early for a final clinical appraisal of the result.

Ballistocardiograms recorded prior to her last operation showed mid-diastolic waves of great amplitude, largest in the vector records but also present in the head-foot record where they equaled the systolic complexes in amplitude.

Records taken 2½ weeks after the last operation showed a decrease in the amplitude of the diastolic waves. Figures 10A and B show records taken in the head-foot position while Figure 10C and D show those taken in the lateral (90° rt.) position. Mid-diastolic waves are insignificant in the two head-foot tracings but are relatively large in the lateral records. Like the preceding case, this patient had a pre-cordial defect through which the heart could be seen to pulsate vigorously; phonocardiograms and apex cardiograms were taken in this area. Phonocardiograms show a clearcut protodiastolic sound coinciding with the beginning of the ballistic diastolic waves (see C). The apex cardiograms show an early diastolic retraction followed by a steep expansion ending in a thrust and a plateau. Like the preceding case the ballistic diastolic waves appear to begin at the nadir of the early diastolic precordial impulse. Simultaneous electrokymograms and ballistocardiograms (electromagnetic) on this patient showed these diastolic waves to begin in the first half of the steep ventricular filling limb.

The last ballistocardiograms taken on this patient, 2½ months after operation, showed further improvement.

COMMENT ON CASES

Of the five cases studied pre-operatively the head-foot ballistocardiogram was abnormal in four; the remaining case (#3) had a normal head-foot ballistocardiogram but abnormal vector records. The feature common to all the cases studied pre-operatively (and most of the post-operative ones) was the presence of abnormal ballistic waves originating during diastole. These waves began shortly after the termination of systole, occupied most of diastole and occasionally continued into the initial portion of the following systole, distorting the systolic complex. In some cases there was distortion of the early part of the systolic complex without obvious "ride-in" from the mid-diastolic waves; this may have been due either to interference produced by abnormal presystolic waves or to an abnormality of early ventricular contraction. The abnormal diastolic waves were characteristically large, often greater than the systolic waves. They were generally more prominent in the vector records (i.e., 30° lt.; 60° rt., lateral or A-P) than in the head-foot and in some instances they were detected *only* in these records. They were subject to rather marked respiratory variation in amplitude; in some cases the diastolic waves were quite large during ordinary breathing but almost disappeared during suspended respiration. The vector loops described by these abnormal ballistic waves

showed considerable individual variation, the reasons for which will be considered later.

Eight of the ten cases presented had one or more ballistocardiograms at varying time intervals following pericardiectomy and these allowed a study of the effects of pericardiectomy on the ballistocardiographic pattern. Two of these eight patients (cases 9 and 10) showed only minor or moderate clinical improvement after operation; in each case the characteristic electrokymographic pattern and the ballistocardiographic abnormality have persisted. The remaining six cases were markedly improved following operation. In three of these (cases 1, 2 and 6) the ballistocardiograms became normal (or nearly so) post-operatively and electrokymograms showed disappearance of the "flat-top and V" pattern. In another (case 7) the post-operative ballistocardiogram was probably normal but the presence of auricular fibrillation made interpretation difficult; electrokymographic findings after operation were equivocal. In one (case 3) the single ballistocardiogram taken post-operatively, 9 weeks after operation, was more abnormal than the pre-operative one; post-operative RKYs showed pulsations of good amplitude but EKYs showed suggestive "flat-tops and Vs" over the lower left ventricle. In the remaining case (# 8) a ballistocardiogram five years after operation was abnormal, showing distortion of the initial portion of the systolic complex, but there were no abnormal early or mid-diastolic waves; post-operative EKYs and RKYs have all been normal. (The type of ballistic abnormality this 56 year old man demonstrated has been seen in apparently normal persons above the age of fifty; it should also be mentioned that in this case the adherent pericardium was removed from the anterior surface of the heart only.)

There was a distinct time lag in the return of the ballistocardiogram to normal in the three cases in which it did so following pericardiectomy. In case 1 a record only 10 days after operation showed that the previously huge mid-diastolic waves had disappeared but there was distortion of the early systolic waves. A record taken $2\frac{1}{2}$ months after operation was practically normal (Figs. 2 and 3). In case 2 a record taken 13 days after operation was still abnormal and showed diastolic waves larger than those in the pre-operative record. However, a record taken $6\frac{1}{2}$ months after operation was essentially normal and showed no significant diastolic waves (Figs. 4 and 5). In case 6 the record one month after operation showed moderately large mid-diastolic waves and evidence of pre-systolic "ride-in" while the record taken $3\frac{1}{2}$ months later had become normal. Thus, in no case did the ballistocardiogram return to normal immediately after operation and in all cases several months elapsed after operation before ballistic form became normal. Moreover, the electrokymogram usually returned to normal before the ballistocardiogram which suggests that some circulatory abnormality was still present in spite of normal movement of the heart borders.

DISCUSSION

The foregoing presentation makes it clear that the ballistocardiogram is altered in constrictive pericarditis. The underlying factors responsible for the unusually large and abnormal diastolic waves are worthy of comment. Since the predominant defect in this condition appears to be an impediment to ventricular filling, rather than to emptying, the intraventricular pressure drops to its usual low level as diastole begins. The combination of a high venous (and auricular) pressure and a low initial ventricular diastolic pressure results in a markedly increased atrio-ventricular pressure gradient which causes a rapid surge of blood into the ventricles early in diastole. Since the ventricular walls are rigid and inelastic and since the position of the heart is often firmly fixed by extra-pericardial adhesions, it is unable to "ride with the blow" and consequently received a sharp impact which is transmitted to the body. (This is not unlike the jolt one receives when he catches a hard-thrown baseball with the arm held stiff.) Moreover, the ventricles fill at an unusually rapid rate (as a result of the high pressure head and the relatively indistensible character of the ventricular walls) so that early in diastole the ventricles reach their limits of distensibility. At this point ventricular pressure abruptly rises to the level of the elevated auricular pressure producing a sharp impact which is probably a "waterhammer" effect. Physiological data derived through the use of other methods (right auricular and ventricular pressure curves and ventricular electrokymograms (9, 10, 14)) suggest that the sudden onset and the abrupt, premature cessation of high velocity ventricular filling produces large surges of blood within the heart and venous system. That such intravascular forces are transmitted to the body is apparent from the precordial displacement curves shown in Figures 9 and 10. Wood (15) has called attention to these precordial diastolic thrusts, which he termed "the diastolic heart beat," and recently presented a ballistocardiogram showing abnormal mid-diastolic ballistic waves in a case with such a phenomenon. Johnston and Overy (16) in their studies of low-frequency precordial vibrations have shown a displacement curve from a patient with constrictive pericarditis which was quite similar to the "flat-top and V" pattern seen in the electrokymogram. There was a rapid outward precordial thrust early in diastole terminating in a plateau which was maintained until the next systole.

Based on the above evidence, one seems justified in concluding that the abnormal early and mid-diastolic waves seen in the ballistocardiogram are due to the abrupt onset of rapid ventricular filling and to its sudden cessation early in diastole.

No comment has been made thus far as to the cause of the distortion in the form of the initial part of the systolic complex so often seen in these cases of constrictive pericarditis. In some records, especially those with rapid pulse

rates, it is obvious that this is due to "ride-in" by oscillations originating in early diastole. In others, however, the systolic distortion either occurs alone or is distinctly separated from the early or mid-diastolic waves, the latter having died out before next systole beigns. Some of the deflections which appear early in systole, usually before the peak of the I wave, are seen to begin in late diastole while in others it is impossible to determine whether they originate late in diastole or very early in systole. It has been indicated earlier that in constrictive pericarditis the ventricles reach their capacity in early diastole after which time they are unable to accept more blood and are relatively "passive" for the remainder of diastole. At the time of auricular systole, the forceful contraction of the auricles, in attempting to pump more blood into the already filled, rigid-walled ventricles might be expected to produce impacts giving rise to presystolic ballistic deflections which would "ride into" and distort the early systolic waves. The apex cardiograms shown in Figures 7, 9 and 10 reveal distinct precordial impulses following the P waves in the electrocardiogram and preceding the QRS complexes and the systolic apical thrusts. The phonocardiograms in Figures 7 and 9 also show low-frequency presystolic deflections. The precordial impacts are presumably due to the forcible contraction of the auricles causing a displacement of the heart forward so that the apex is thrust against the chest wall, a not unlikely assumption since we have recorded small apical thrusts following the P waves in cases of complete heart block. In addition, it seems likely that the blood within the auricles, being unable to enter the filled ventricles, would be ejected back into the venous system. Thus, the sudden displacement of the heart and the regurgitation of blood back into the venous system, both produced by auricular contraction, may account for the late diastolic-early systolic deflections under consideration. There is no conclusive proof for this hypothesis, however, and it is possible, in the cases where these waves appear to begin simultaneously with the onset of systole, that factors involving ventricular contraction are concerned. The case of constrictive pericarditis published by Starr (Fig. 4, E.1, E.2) in (17) suggests that such a mechanism exists, for the presence of auricular fibrillation in his patient allows the influence of auricular contraction to be dismissed. A ballistocardiogram taken prior to pericardiectomy in this case showed large mid-diastolic waves but no definite distortion of the systolic complex. Two months following operation, which produced great clinical improvement but no change in cardiac rhythm, abnormal mid-diastolic waves (altered in form) were still present and the initial portion of the systolic complex was distorted by an additional distinct footward wave. These complexes are similar to those shown in Figures 8 (H-F) and 9. It is interesting that our case which showed this feature to the most striking degree was, like Starr's, post-operative. Indeed, early systolic abnormality was an almost constant feature in our post-operative

records, especially those taken shortly after operation. The question as to whether this systolic distortion is due to "ride-in" by diastolic waves or is due to abnormalities of ventricular contraction is more than an academic one for it would seem important to have some information regarding the impediment to systolic ejection as well as that to diastolic filling. Unfortunately, such a decision cannot be made from the available data and must await further investigation.

The spatial distribution of the body movements produced by the abnormal diastolic impacts in constrictive pericarditis differs somewhat from one individual to another. It is presumed that these differences are due to differences in anatomical position of the heart, site of most marked constriction, and the degree and manner of fixation of the heart to the mediastinum and thoracic cage.

The ballistocardiographic changes which are under discussion are probably not specific for constrictive pericarditis. Abnormal ballistic diastolic waves have been described in a variety of conditions including hypertension (17), congestive heart failure (18), A-V fistula (19) and gallop rhythm (18), (20); the presence of such waves usually suggests advanced heart disease (17). We have observed late diastolic waves (with "ride-in" into systole) in presystolic gallop rhythm and in coronary artery disease but have also seen them in apparently normal older people. Abnormal diastolic waves of all types are presumably associated with abnormal or altered ventricular filling.

While diastolic waves of considerable magnitude are seen in other conditions we have been impressed with the great size of these deflections in most of our cases of constrictive pericarditis. This is believed to be due to an unusual, if not unique, set of hemodynamic conditions. The combination of the high venous pressure coupled with the normal (or nearly so) initial ventricular diastolic pressure seen in constrictive pericarditis (10) is probably shared only with mitral stenosis and tricuspid stenosis. In both of these cases, of course, there is inflow obstruction which prevents rapid ventricular filling. Furthermore there is no abrupt cessation of filling in these cases which, unlike those of constrictive pericarditis, benefit by a prolongation of diastole.

The cause of the lag in the return of the ballistocardiogram to normal following operation can only be speculated on. Blalock and Burwell (2) commented on the lag in the return of normal circulatory function after operation and suggested that this represented the time required by an atrophic myocardium to return to normal. Sellors (4) pointed out that a satisfactory pericardiectomy may result in a lowering of venous pressure and a reduction of liver size and ascites within a few weeks but "full and final improvement should not be expected within twelve to eighteen months." That the heart and circulation do not return to normal immediately after removal of the constricting

pericardium is suggested by Hansen's finding of persistence of the "early diastolic dip" pattern in a pressure curve obtained by direct needle puncture of the right ventricle immediately following an adequate pericardiectomy in a patient with constrictive pericarditis (10). It seems reasonable to assume that an appreciable period of time is required for the heart muscle to regain its normal "tone," elasticity and strength after having been confined by its constricting fibrous shell for a long period of time. Our ballistocardiographic findings would tend to support this assumption. Inadequate pericardiectomy or irreversible myocardial changes, such as fibrosis and calcification, are probably responsible for the continued persistence of ballistocardiographic abnormality after operation.

The use of the ballistocardiograph should have particular value in the study of constrictive pericarditis since this disease occurs so often in young people whose ballistocardiograms have not been rendered abnormal by other factors such as aging and coronary disease.

SUMMARY

1. Ten cases of constrictive pericarditis were studied before and/or after pericardiectomy by means of conventional and vector ballistocardiography.

2. The conventional head-foot ballistocardiogram was abnormal in four of the five cases studied prior to pericardiectomy; in the remaining case only the vector records were abnormal.

3. The ballistocardiographic abnormality common to all of the preoperative cases was the presence of large abnormal early and mid-diastolic waves. In addition, in most instances, there was distortion of the initial portion of the systolic complex.

4. Reasons are given for believing that the large diastolic waves are due to impacts produced within the rigidly encased heart by the abrupt onset of high velocity ventricular filling and by its sudden termination in early diastole.

5. The abnormal diastolic waves were more apparent, and in some instances were observed only, in the ballistocardiographic vector records.

6. Three cases were studied before and after operation and in two of these the huge diastolic waves present in pre-operative records were absent in late post-operative records which become relatively normal. In the third a single early post-operative record showed persistence of ballistic abnormality.

7. Eight of the patients were subjected to pericardiectomy and six were markedly improved or cured. Of these six, post-operative ballistocardiograms became normal in three and probably normal in another. One was not studied late post-operatively and one showed only persistent early systolic distortion. The two patients who received only slight or moderate benefit from the oper-

ation showed persistence of their abnormal ballistocardiographic and electrokymographic patterns.

8. There was a lag of several months in the return of the ballistocardiogram to normal in those cases in which it did so after pericardiectomy.

9. It is suggested that ballistocardiography may be useful in the diagnosis of constrictive pericarditis and in the evaluation of results of pericardiectomy.

The ten cases in this study are among those reported by one of us elsewhere (9, 13.) The following is a list of these cases identified by our case number, the patient's initials and the case number of the patient in the other reports:

Case 1 (C. M.) #5; Case 2 (L. N.) #6; Case 3 (L. W.) #4; Case 4 (W. M.) #10; Case 5 (N. D.) #9; Case 6 (W. B.) #7; Case 7 (R. McA.) #2; Case 8 (E. C. P.) #17; Case 9 (J. H.) #13; Case 10 (G. V. S.) #14.

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MECHANISMS OF FLUID AND ELECTROLYTE RETENTION IN EXPERIMENTAL PREPARATIONS IN DOGS

I. Acute and Chronic Pericarditis

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INTRODUCTION

In recent years, considerable attention has been directed to the problem of fluid and electrolyte retention in certain syndromes and diseases. In congestive heart failure and cirrhosis of the liver, excretion of salt and water by the kidney may be markedly reduced (1–8). Fluid and electrolyte retention has been related to such factors as elevated venous pressure (9, 10), low rate of glomerular filtration (1, 2, 11), and hyperadrenocortical activity (12) in patients with cardiac failure and to altered adrenocortical function (8, 13) in cirrhotics. The evidence for these factors is only suggestive and the mechanisms by which they operate are not completely understood (14).

Most studies of mechanisms of salt and water retention in experimental animals have been limited to acute and subacute preparations (9, 15–19). Factors operating in acute preparations, particularly under anesthesia, may differ from those present in chronic experimental disease in which an interplay of homeostatic mechanisms may occur. Dogs with experimental pericarditis live for several months and accumulate large depots of extracellular fluid as edema and ascites (20, 21). In the present report, venous pressure and glomerular filtration rate have been studied in relation to electrolyte and water balances in experimental pericarditis. The observations have been evaluated in an attempt to explain the pathogenesis of edema and ascites in this preparation. This information may be of value in elucidating mechanisms of fluid and electrolyte retention in clinical states.

METHODS

Production of pericarditis

Cellophane 300 PUT-71 from DuPont[1] was implanted into the pericardial cavity in thirteen dogs. After anesthetization with sodium pentobarbital, the pleural cavity was en-

[1] The cellophane was supplied through the courtesy of A. S. Taylor of the Technical Service Laboratory, Cellophane Division, E. I. DuPont de Nemours & Co., Wilmington, Delaware.

tered through the 5–6th interspace. In dogs 1, 2A, 7, 8, 9, and 10 cellophane was placed upon the surface of the right auricle and ventricle. In cases 2, 3, 4 ,5, 6, 11, and 12 the entire surface of the heart was enveloped. The exact location of the cellophane was verified by autopsy. Cellophane was applied as folded sheets which were sewed securely to the parietal pericardium to prevent displacement. Adequate drainage of pericardial fluid prevented fatal acute cardiac tamponade and chronic preparations were obtained.

Experimental material and design

The experiments were performed on trained unanesthetized dogs; all were females which had been previously perineotomized to expose the urethral meatus with the exception of two males (dogs 1 and 2A). Preliminary studies were conducted on dogs 1–4 to develop the surgical technique for producing pericarditis and to ascertain the important functional changes. The plan for the definitive study consisted of observations during a 3 or 4 week control interval and the experimental period in dogs 5–12. The study in dog 2A was limited to the chronic stage of the experimental pericarditis. Measurements included creatinine (CR) and para-aminohippurate (PAH) clearances, sodium (Na), chloride (Cl), nitrogen (N), and water balances, plasma Na and Cl, T-1824 dye space, hemoglobin, hematocrit, plasma proteins, body weight, arterial and right ventricular pressures, and central and peripheral (external jugular and femoral) venous pressures. Potassium (K) balance and plasma K were studied in dogs 9–12 and 2A.

Three postabsorptive renal clearance periods were carried out on three occasions at intervals of approximately one week during the control period and at similar intervals during the experimental period. In addition to postabsorptive clearance studies, postprandial measurements were made in two dogs During the morning of the postabsorptive renal clearances, plasma electrolytes, arterial and venous pressure, heart rate, body temperature, and T-1824 dye space were determined One control measurement of right auricular and ventricular pressure was made. Three or four urine and two or three fecal collections were made during the control period; balance studies were conducted continuously during the experimental period Body weight was determined daily.

Experimental procedures

Renal clearances. Effective renal plasma flow (RPF) and glomerular filtration rate (GFR) were measured by determining C_{PAH} and C_{CR} using a constant infusion of CR and PAH in normal saline at a rate of approximately 0.3 cc./min.[2] For the postabsorptive studies, no water was allowed after 5 P.M. on the day before the clearance procedure. For the postprandial measurements, 500 cc. of water were given by stomach tube with the meal. Renal clearance studies were not made in the presence of fever except in one instance (dog 7 on August 12).

Balance studies. Dogs were kept in metabolic cages except during experimental procedures. A synthetic diet containing 80 Cal./kg./day, .2 gm. of N/kg./day and 4 m. eq. of Na/kg./day[3] was given to dogs 7–12 and 2A. Dogs 5 and 6 received the same amount of N and

[2] In the preliminary study (dogs 1–4), renal clearances were performed following a single injection of PAH and after the oral administration of CR.

[3] The value of 4 m. eq. of Na/kg./day was used because preliminary studies indicated that a 15 kg. dog could tolerate the accumulation of ascites at the rate of .2–.4 kg. daily (Figure 1). Four tenths of a kg. of ascitic fluid contained approximately 56 m. eq. of Na so that an intake of 4 m. eq. of Na/kg. allowed a 15 kg. dog to gain slightly more than .4 kg./day.

calories, but Na intake was limited to .5 m. eq./kg./day. Some animals ingested the diet voluntarily while others were forced fed to obtain a known constant intake. The diet was analyzed for N, Na, K, and Cl at frequent intervals Daily urine specimens were collected in Mason jars containing 20 cc. of 10% sulfuric acid and 20 cc. of toluene; the cages were washed daily with distilled water which was included in the collection specimen. Urine collection periods were begun and terminated by bladder catheterization. Feces were collected in Mason jars containing 300 cc. of concentrated sulfuric acid and 100 cc. of distilled water. Carmine or rectal enemata were used to mark the beginning and end of fecal collection periods.

Cardiovascular pressure measurements. Femoral arterial blood pressure was measured by direct puncture with a #20 needle attached to a strain gauge and a Cambridge string or a D'Arsonval galvanometer. Phases of respiration were recorded simultaneously with arterial pressure except in cases 5–7. Right auricular and ventricular pressures were recorded by means of an intracardiac catheter attached to the arterial manometric system; for these measurements the sensitivity of the arterial manometer was increased. External jugular and femoral venous pressure were measured with a saline manometer. Venous and intracardiac pressures were referred to a level 6 cm. above the table surface.

Other measurements. T-1824 dye space was determined by a modification of the method of Gregersen and Stewart (22) unless hemolysis or lipemia was present; in this event, the acetone procedure of Chinard & Eder (23) was used. Hematocrits were determined by the method of Wintrobe (24). Body weight was measured with a Howe scale with an error not exceeding ±1 oz.

Chemical methods

PAH was determined in trichloroacetic acid filtrates and diluted urine according to the method of Smith (25). Plasma filtrates and diluted urine were analyzed for creatinine by a modified method of Folin (26). Filtrates for creatinine were prepared by protein precipitation with tungstic acid in dogs 1–4, cadmium sulfate and sodium hydroxide in dogs 5–7, and trichloroacetic acid in all other dogs.[4] Plasma and urine chlorides were determined by iodometric titration (27). Chlorides in food and feces were analyzed by a modified Volhard technique (28). Na and K were determined by internal standard flame photometry (29–30) with an error not exceeding 2%. Aliquots of food and feces were leached with nitric acid, diluted, and analyzed for Na and K. Comparison of leaching with ashing showed adequate agreement and recoveries after leaching were satisfactory. The N content of food, feces, urine, plasma, and ascitic fluid was determined by a micro-Kjeldahl method (31). Hemoglobin was determined on blood by the method of Evelyn (32).

RESULTS

1. *Control data*

In chronic studies of cardiovascular and renal hemodynamics and electrolyte excretion, it is preferable for each dog to serve as its own control, and this design has been followed except for dog 2A. It is desirable for the renal clear-

[4] In establishing the validity of the chemical methods for the definitive study, recoveries of creatinine from plasma utilizing tungstic acid precipitation were consistently low. Cadmium sulfate and sodium hydroxide precipitation yielded satisfactory recoveries but the occasional occurrence of a fine precipitate necessitated repeated adjustment of the pH of the reagents and repeat determinations of plasma creatinine. These difficulties were eliminated by using tricloroacetic acid as a protein precipitant.

ance procedure and the dietary regimen to be identical during the control and the experimental periods. These considerations are extremely important in evaluation of chronic changes in GFR and RPF because of the lability of these functions in the dog. The level of renal hemodynamics is a function of several variables including the amount of protein ingested (11, 33–35) and the extent of hydration and salt loading (11, 36, 37) during the renal clearance procedure. Tabulated data of renal hemodynamics in normal dogs obtained under a variety of circumstances (38) are of limited value for comparison with data from studies of chronic experimental preparations.

In order to show the reproducibility of the renal clearance measurements from one week to the next and to evaluate the findings in case 2A, control data are summarized in Table I. Observations of venous, right auricular, and right ventricular pressure, femoral arterial pressure, hemoglobin, hematocrit, T-1824 dye space, plasma proteins, body weight, C_{CR}, C_{PAH}, filtration fraction (FF), and fecal Na and K excretion are tabulated. Each value for venous pressure, hemoglobin, hematocrit, T-1824 dye space, plasma proteins, and fecal electrolytes is the average of three control determinations. The value for C_{CR} and C_{PAH} for each week is the average of three clearance periods. The lowest arterial pressure recorded during the control period was used for tabulation.

2. *The effect of the sham operation*

Since the experimental preparations for this study were made surgically, a sham operation was performed to ascertain the extent of the changes attributable to the operative procedure. After a 3 or 4 week control study, a thoracotomy was performed on two dogs using the same procedure as during the production of pericarditis except that the heart and pericardial cavity were not disturbed. Na, Cl, and water balances were positive from 1 to 3 days whereas N and K balances were negative from 1 to 2 days. A decline in hemoglobin and hematocrit and an elevation in T-1824 dye space accompanied the retention of salt and water. Plasma Na and Cl dropped slightly on the first postoperative day but returned to the control level within 3 or 4 days. Renal clearance determinations on the third postoperative day in one dog and on the sixth postoperative day in the other revealed no alteration in GFR or RPF. Renal clearances were not performed earlier postoperatively because of the slight elevation in body temperature which followed surgery. Venous and arterial blood pressure remained at the control level. The principal changes in the dog which showed the greater response to the surgery are shown in Figure 2.

3. *Clinical course of experimental pericarditis*

The course of the experimental period appeared to be the same regardless of whether cellophane was implanted over the right auricle and ventricle or around the entire heart. Isaacs (39) has also found that irritative material

TABLE I

Control Data

DOG NO.	BODY WEIGHT	VENOUS PRESSURE		MEAN RIGHT AURICULAR PRESSURE	RIGHT VENTRICULAR PRESSURE	ARTERIAL PRESSURE	PLASMA PROTEIN	HEMOGLOBIN	HEMATOCRIT	T-1824 DYE SPACE	C_{CR}				C_{PAH}				FF	FECAL Na EXCRETION	FECAL K EXCRETION
		External Jugular	Femoral								1st week	2nd week	3rd week	Average	1st week	2nd week	3rd week	Average			
	kg.	*mm. water*	*mm. water*	*mm. water*	*mm. Hg*	*mm. Hg*	*gm. %*	*gm.%*	*%*	*cc.*	*cc./min.*				*cc./min.*				*%*	*m.eq./day*	*m.eq./day*
P-7	18.5	72	—	0	36/0	155/96	7.1	16.5	51	817	45.8	46.4	45.4	45.9	145	136	144	142	32	3.9	—
P-8	18.8	75	119	34	35/2	177/96	6.5	17.3	55	717	50.1	48.6	42.7	47.1	149	139	121	136	35	4.7	—
P-9	19.4	102	84	38	36/3	188/110	5.9	18.5	57	811	42.6	48.1	42.7	44.5	146	154	140	147	30	2.9	.7
P-10	18.8	96	101	—	—	187/90	6.3	17.3	56	580	46.0	55.5	46.7	49.4	154	178	157	163	30	3.5	.9
P-11	15.4	53	68	57	33/3	160/87	6.6	18.2	55	710	45.2	47.8	45.1	46.0	153	143	132	143	32	4.9	1.6
P-12	23.1	52	100	56	34/4	143/85	6.7	16.9	52	1116	59.7	55.1	50.9	55.2	179	171	161	170	33	5.6	1.4
IVC-1*	15.0	59	51	40	28/3	183/101	6.7	15.8	49	710	51.0	48.0	47.7	48.9	150	139	143	144	34	6.2	1.5
IVC-2	15.3	40	83	25	46/0	144/82	6.5	13.2	51	831	49.9	51.8	53.0	51.6	154	148	151	151	34	5.7	1.3
IVC-3	15.3	60	72	16	48/2	167/82	5.9	16.9	44	707	31.2	40.8	31.1	34.4	105	130	98	111	31	4.7	1.4
Mean	17.7	68	85	39	37/2	167/92	6.5	16.7	52	778	46.8	49.1	45.0	47.0	148	149	139	145	32	4.7	1.3

* The three dogs designated IVC-1–3 were the material for another study; however, the experimental plan was identical during the control period in the study of dogs IVC 1–3 and dogs P 7–12 of the present study.

covering the right heart or enveloping the entire organ produced the same syndrome. More important than the location of the cellophane was the marked individual variation in the inflammatory reaction.

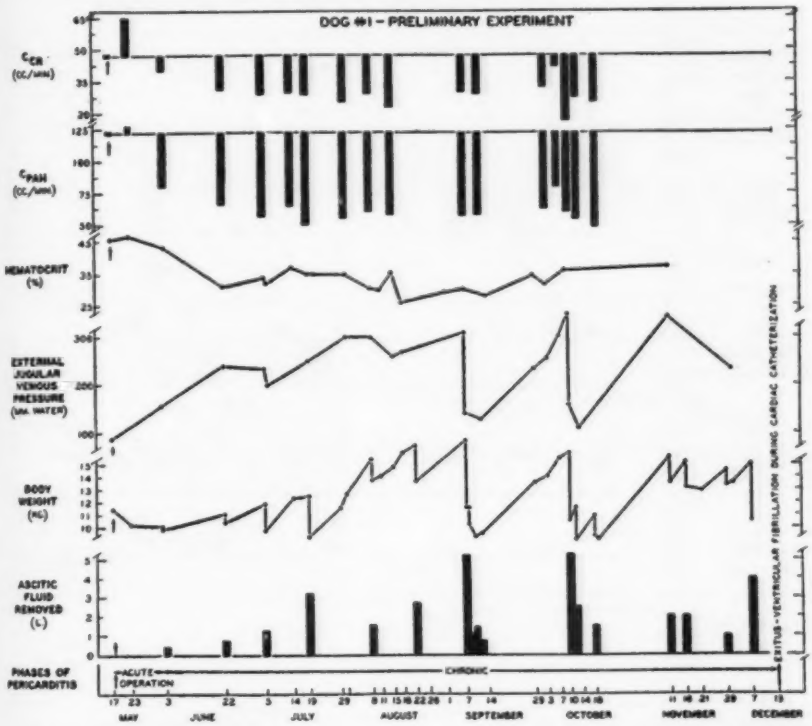

FIG. 1. *Preliminary study of acute and chronic experimental pericarditis.* Experimental values for C_{CR} and C_{PAH} were plotted as solid columns from a horizontal line which represents the control level. The vertical arrows indicate the date of the operation (cellophane implantation) and exitus.

The most commonly observed course (dogs 1, 2, 3, 4, 7, 11, and 2A) was characterized by an acute and a chronic period of fluid and electrolyte retention (Figures 1, 3). The acute phase usually lasted from 10 to 12 days; this phase was terminated by a spontaneous diuresis. Salt and water retention was manifested clinically by peripheral edema which proceeded to anasarca occasionally. In the chronic stage, edema was present but ascites was the principal depot for storage of electrolytes and water. In dog 11, daily exhaustive exercise was necessary to maintain a positive balance for salt and water during the chronic stage. The experimental period lasted as long as six months.

The remainder of the animals failed to develop ascites. In dogs 6 and 9, a spontaneous diuresis occurred at the end of the acute phase and a period of

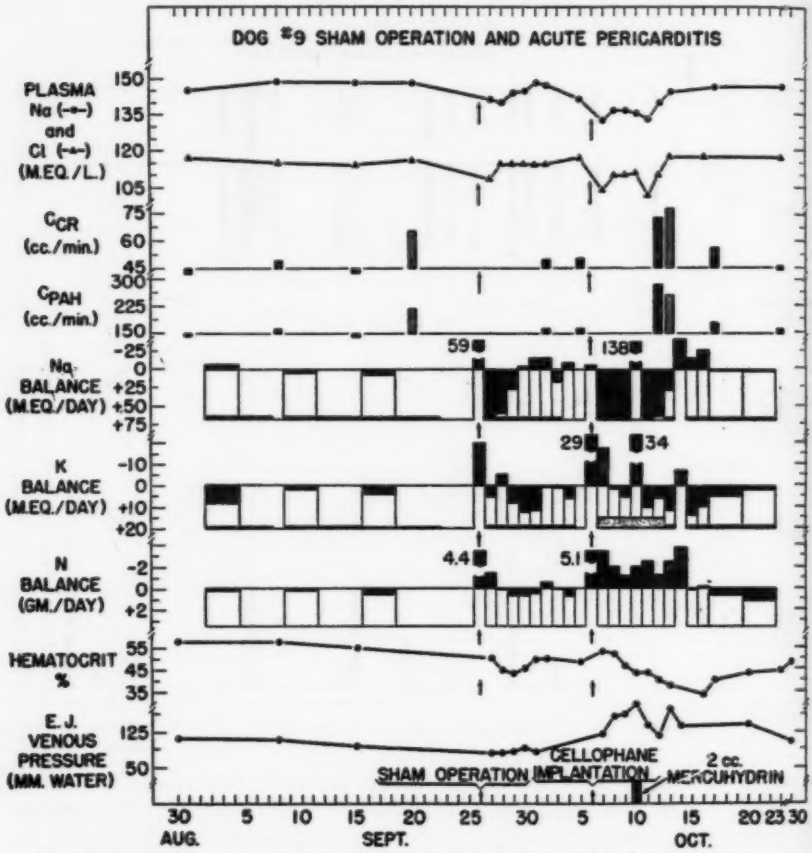

FIG. 2. *Comparison of the changes following a sham operation with alterations during acute experimental pericarditis.* The horizontal line from which determinations for C_{CR} and C_{PAH} were plotted represents the average control value for the post absorptive renal clearances. Solid columns indicate post absorptive values for C_{CR} and C_{PAH} while diagonally hatched columns show values for postprandial measurements. The convention for the balances is as follows: (1) intake was plotted downward from the zero line, (2) output was plotted upward from the intake line, (3) solid black areas represent total balances, and (4) the stippled areas show fecal Na and K output. The vertical arrows indicate the date of the sham operation and cellophane implantation. E. J. is the abbreviation for external jugular.

inactive pericarditis without fluid retention followed. In others, exitus occurred during the acute stage (dogs 5, 8, 12) or death resulted from anesthesia (dog 10).

4. *Alterations in individual functions*

Venous, right auricular, and *right ventricular pressure.* Progressive elevation in peripheral (external jugular and femoral) venous pressure occurred during

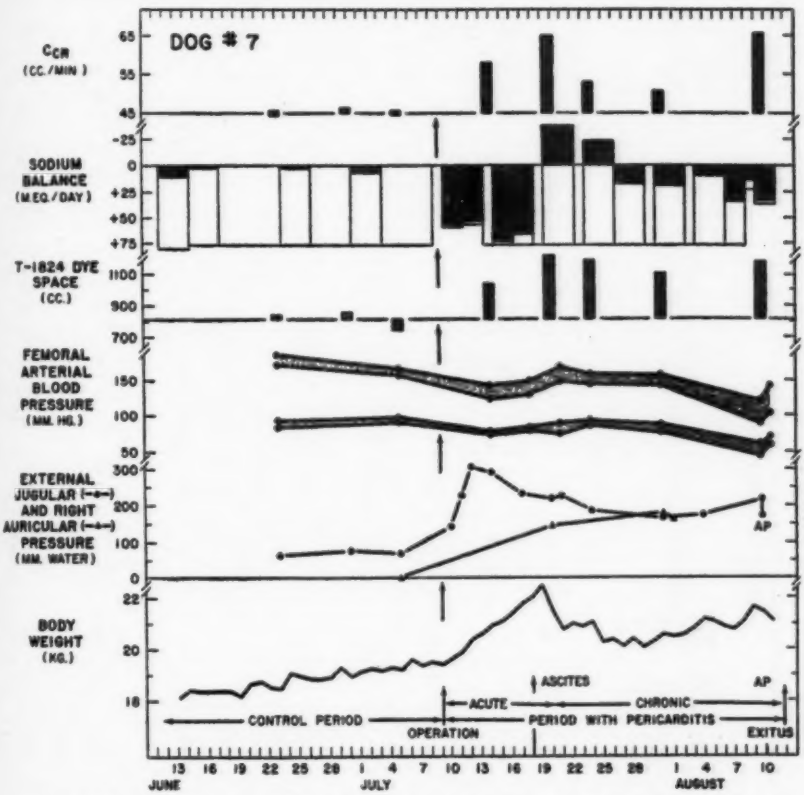

FIG. 3. *Changes in acute and chronic experimental pericarditis.* The horizontal line from which values for T-1824 dye space were plotted represents the average control value. The stippled areas show the decrease in systolic and diastolic pressure with inspiration. See Figure 2 for description of other symbols and convention for sodium balance. The vertical arrows indicate the date of the operation (cellophane implantation), the appearance of ascites, and exitus. AP indicates abdominal paracentesis. Additional data from the study of dog 7 are presented in Tables II and III.

the acute phase. This rise began on the first or second postoperative day and reached levels as high as 300 mm. of water (Figure 3). After the inflammatory reaction to the cellophane subsided, systemic venous pressure declined, but it remained 160 mm. of water or higher in chronic preparations that formed ascites (Figures 1, 3, 4). With the accumulation of ascitic fluid, venous pres-

TABLE II

Cardiovascular Pressures, Hemoglobin, Hematocrit, T-1824 Dye Space, Plasma and Ascitic Fluid Proteins, Plasma Electrolytes, and Renal Function in Experimental Pericarditis (Dog 7)

DATA	OBSERVATIONS AND EXPERIMENTAL PROCEDURES	EXTERNAL JUGULAR VENOUS PRESSURE	MEAN RIGHT AURICULAR PRESSURE	RIGHT VENTRICULAR PRESSURE	ARTERIAL PRESSURE	HEMOGLOBIN	HEMATOCRIT	T-1824 DYE SPACE	PLASMA PROTEINS	ASCITIC FLUID PROTEINS	PLASMA Na	PLASMA Cl	C_{CR}	C_{PAH}	FF
Control Period															
		mm. water	*mm. water*	*mm. Hg*	*mm. Hg*	*gm.%*	*%*	*cc.*	*gm.%*	*gm.%*	*m.eq./l.*	*m.eq./l.*	*cc./min*	*cc./min.*	*%*
June 23.....		65			176–194* / 86–94	17.0	51	846	7.4		144	116	46	145	32
June 30.....		80				16.5	54	859	7.0		143	113	46	136	34
July 5.....		72	0	36/0	158–169 / 93–98	15.9	49	745	7.0		143	113	45	144	31
Experimental Period															
July 9.....	Cellophane Implantation														
July 10.....		150				15.5	54				130				
July 11.....		238				14.2	46				124	104			
July 12.....		300				13.7	43								
July 14.....		285			125–146 / 73–78	12.4	43	1040	6.3		134	109	59	198	30
July 17.....		245				10.7	35								
July 18.....	45 cc. of ascitic fluid removed for analysis				132–152 / 80–84					2.8					
July 20.....		215	145	36/10	126–141 / 87–93	10.5	35	1220	5.4		152	118	66	177	37
July 21.....		220													
July 24.....		180			148–160 / 88–93	11.7	37	1198	5.9		146	117	54	150	36

July 24.....		180			148–160 88–93	11.7	37	1198	5.9		146	117	54	150	36
July 31.....		178	180		145–158 78–89	11.7	42	1105	6.2		147	116	52	140	37
August 1....			164	27/13											
August 4....	20 cc. of ascitic fluid removed for analysis	160				10.6	35			4.7	150	117			
August 10...	After control observations 945 cc. of ascitic fluid removed and observations repeated.	210			90–123 43–61	11.4	39	1185	5.9	4.8	140	113	67	182	37
		175			105–140 59–65						143		66	192	34
August 11...					101–143 57–67										
August 12...	Exitus. 975 cc. of ascitic fluid removed at autopsy									4.7	120				

* The range in systolic and diastolic pressure is the variation in pressure with respiration.

sure became further elevated; following abdominal paracentesis, tension in the systemic veins fell (Figure 1, 3, 4). The most marked changes were observed in dog 1 (Figure 1); external jugular and femoral venous pressure reached a level of 350 mm. water and fell to 120 mm. water following removal of 7700 cc. of ascitic fluid.

Mean right auricular and right ventricular diastolic pressure were elevated during both phases of pericarditis and the pressure gradient between the peripheral veins and heart was decreased (Table II). Observations on dog 2A on the day before death revealed a mean auricular pressure of 250 mm. of water and a right ventricular pressure of 30/18 mm. Hg (see Table I for normal values).

Femoral arterial pressure and heart rate. During the acute phase of pericarditis a drop in systolic and diastolic pressure occurred (Figure 3). This depressor response was accompanied by a fall in systolic and diastolic pressure during inspiration and a rise during expiration; the variation with respiration was greater than during the control period.[5] Termination of the acute phase was associated with a return in pressure to the control level but the so-called "paradoxical pulse" remained. During the chronic period blood pressure was maintained until pre-terminally (Figures 3 and 4). Heart rate increased from a basal level of 80–100 beats/min. to 140–180 beats/min.

Body weight and *metabolic balance data.* During the acute phase, body weight increased in accordance with the positive Na, Cl, and water balances (Figures 2 and 3 and Table III). The spontaneous diuresis which terminated the acute phase was accompanied by negative balances and a decline in body weight. In dog 7, this diuresis occurred in the presence of a venous pressure of 250 mm. of water and ascites (Figure 3). When ascites developed, diuresis was followed by the chronic period of fluid retention with positive Na, Cl, and water balances and a gain in body weight (Figures 3 and 4 and Table III). Marked variations in body weight were associated with the accumulation of ascites and abdominal paracentesis (Figure 1). The principal reduction in Na and Cl excretion was accomplished by the kidney; however, a five to ten-fold decrease in fecal Na excretion occurred (Figure 2 and Table III). In case 2A (Figure 4), fecal Na excretion during the chronic phase ranged from .7 to 1.3 with an average of 1.0 m. eq./day (see Table I for normal values). Changes in Na and Cl balances in these preparations occurred at the same time and in the same direction (Table III).

K balance was negative during the first one or two postoperative days (Figure 2). A short period of positive balance followed but equilibrium was achieved unless ascites developed. In this event, observations during the chronic phase of the experimental period showed a reduction in the renal ex-

[5] The increased variation in the peripheral pulse with respiration has been referred to as a "paradoxical pulse" but as pointed out (40) this term may be a misnomer.

cretion and an increase in the fecal output of K; total balance was slightly positive (Figure 4). When Na balance was markedly positive during the acute phase (Figure 2), fecal K excretion was elevated. Consequently, a markedly

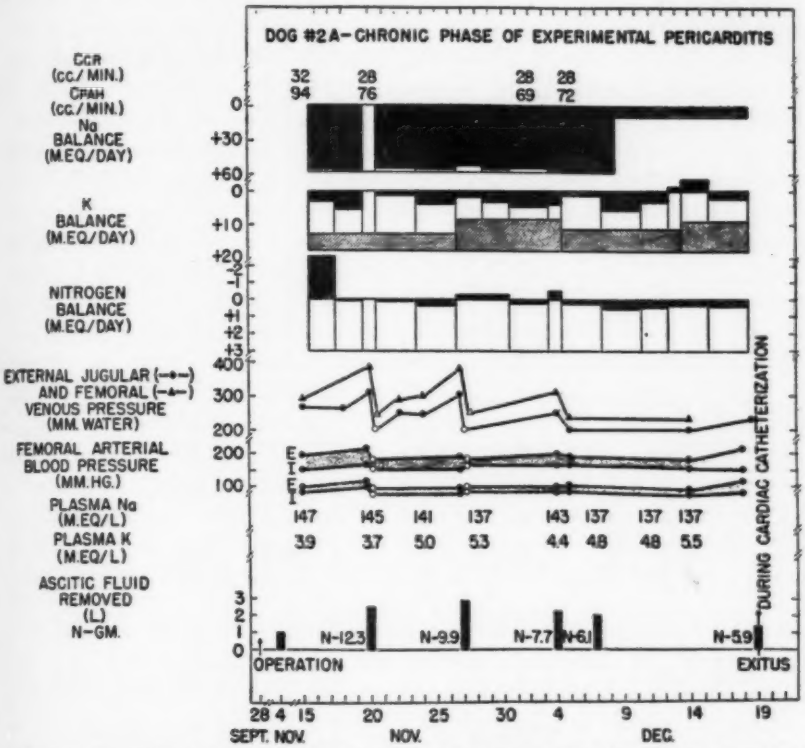

FIG. 4. *Observations during chronic experimental pericarditis.* For description of symbols and convention for balances, see Figures 1–3. The diagonally hatched area for K balance indicates fecal K excretion. Clear circles and triangles for venous and arterial pressure represent determinations made immediately after abdominal paracentesis. The values to the left of the solid columns for the volume of ascites removed indicate the number of gms. of N in the ascitic fluid. The vertical arrows indicate the date of the operation (cellophane implantation) and exitus. Erratum—under nitrogen balance m.eq./day should be gm./day.

positive Na balance during both phases of pericarditis was accompanied by low fecal Na and high fecal K excretion.

Nitrogen balance was negative during the first few days of the acute phase. The duration and extent of the negative N balance appeared to be related to the severity of the pericarditis. The most marked changes were observed in case 9 (Figure 2) in which the dog almost succumbed from pulmonary congestion. In case 11, the reaction to the cellophane was minimal and the changes

TABLE III

Alterations in Body Weight and Metabolic Balances During Experimental Pericarditis (Dog 7)

DATE	BODY WEIGHT	NITROGEN				SODIUM				CHLORIDE				WATER		
		Intake	Output		Balance	Intake	Output		Balance	Intake	Output		Balance	Intake	Urinary Output	Balance
			Urine	Feces			Urine	Feces			Urine	Feces				
Control Period																
	kg.	*mgm./day*				*m.eq./day*				*m.eq./day*				*cc./day*		
June 12–14	18.1	4195	3100	639	+456	76.0	64.9	4.7	+6.4	85.5	81.6	.7	+3.2	751	547	+204
June 15–17	18.4	4195	3050	639	+506	76.0	70.5	4.7	+.8	85.5	84.2	.7	+.6	593	550	+43
June 24–26	19.0	4195	3133	466	+596	76.0	71.3	4.4	+.3	85.5	87.6	1.2	−3.3	843	552	+291
July 1–3	19.3	4195	2994	394	+807	76.0	67.9	2.3	+5.8	85.5	84.4	.7	+.4	674	427	+247
Experimental Period																
July 9	Cellophane Implantation															
July 10–11	20.1	3258	5730	373	−2845	58.5	1.0	.3	+57.2	66.3	3.6	.1	+62.6	986	407	+579
July 12–13	20.8	3148	3461	373	−686	57.0	1.4	.3	+55.3	64.2	24.1	.1	+40.0	1002	625	+377
July 15–16	21.7	4195	3269	528	+398	76.0	1.1	2.3	+72.6	85.5	27.4	.0	+58.1	1363	750	+613
July 17–18	22.4	4195	2928	528	+739	76.0	7.7	2.3	+66.0	85.5	31.6	.0	+53.9	1373	812	+561
July 19	23.1															
July 20–22	21.7	4195	2827	633	+735	76.0	110.6	3.3	−37.9	85.5	120.3	.0	−34.8	851	845	+6
July 24–26	20.9	4195	3048	633	+514	76.0	96.8	3.2	−24.0	85.5	114.7	.6	−29.8	761	785	−24
July 27–29	20.4	4195	2920	633	+642	76.0	50.6	3.2	+22.2	85.5	64.9	.6	+20.0	907	660	+247
July 31–August 2	20.9	4195	2693	775	+727	76.0	48.6	8.0	+19.4	85.5	65.7	1.9	+17.9	1026	685	+341
August 4–6	21.5	4195	2339	644	+1212	76.0	58.8	7.5	+9.7	85.5	74.1	1.8	+9.6	953	590	+363
August 7–8	21.4	4195	2223	644	+1328	76.0	34.2	7.5	+34.3	85.5	46.8	1.8	+36.9	1360	572	+788
August 9	22.1	1277	4325	644	−3692	23.1	2.5	7.5	+13.1	26.0	5.0	1.8	+19.2	696	350	+346
August 10–11	21.5	2032	4080	458	−2506	36.8	1.9	1.4	+33.5	41.5	2.7	1.4	+37.4	1209	189	+1020

* Water balance = intake − urinary output.

in N balance were no more than those observed following the sham operation on dog 9.

During the chronic phase, marked protein depletion occurred in dogs 1 and 2A. Appearance curves for T-1824 dye in ascitic fluid suggested that albumin passed from plasma into the ascites. The protein content of the ascitic fluid was high, ranging from 2.6 to 4.8 gm.%. Protein depletion resulted from loss of ascitic fluid protein which was removed by paracentesis. Plasma proteins fell to 4.2 and 4.1 gm.% in dogs 1 and 2A respectively (see Table I for normal values). In dog 2A (Figure 4), N balance was negative throughout the period of observation. From Nov. 20 to Nov. 27, this animal lost 9.9 gms. of protein N into the ascitic fluid. Inclusion of this ascitic fluid N into the balance calculations results in a negative balance of approximately 1.4 gm. N/day for this period. Furthermore, plasma proteins decreased from 5.5 to 4.1 gm.% during the month of study of dog 2A. In case 7, the duration of the chronic period and the rate of ascites formation were insufficient to result in chronic protein depletion. However, terminally, when ascites formation proceeded more rapidly, N balance became markedly negative.

Hemoglobin, hematocrit, and *T-1824 dye space.* A fall in hemoblobin and hematocrit and a rise in T-1824 dye space occurred consistently during the acute phase (Figure 2 and 3 and Table II). The spontaneous diuresis was accompanied by an increase in hemoglobin and hematocrit and a decrease in T-1824 dye space. If ascites developed, fluid retention again ensured and these functions showed further evidence of hemodilution (Figure 3 and Table II).

Plasma electrolytes. A decrease in plasma Na and Cl occurred during the first 1 to 3 days postoperatively (Figure 2 and Table II). This change was followed by a progressive elevation of the plasma concentration of both electrolytes to the control level. In dog 9, a second decline in Na and Cl occurred following the administration of 2 cc. of mercuhydrin. A significant change in plasma K was not detected during the acute phase except for a decrease following mercuhydrin in dog 9. During chronic pericarditis plasma Na and Cl were maintained at the control level until pre-terminally in dog 7. A slight drop in Na and Cl and an elevation in K occurred in dog 2A.

Renal clearances. A characteristic pattern of alteration in renal function was observed during the acute phase (Figures 1–3 and Table II). Postabsorptive clearances of CR and PAH were elevated; FF was slightly reduced or unchanged.

Since GFR increases after feeding and the principal part of the salt load from the meal is excreted at this time in the dog (41),[6] it seemed important

[6] Repeated studies were made on two dogs for 8 to 10 hours after feeding during the control period; GFR and salt excretion reached a peak from 5 to 8 hours after the meal.

to compare the maximal rate of glomerular filtration after feeding during the control and experimental periods. Observations in two dogs revealed that postprandial renal function was higher during the experimental period (Figure 2). Therefore, it can be concluded with more certainty than from postabsorptive clearances alone that a reduction in GFR was not causally related to increased tubular reabsorption of Na, Cl, and water during the acute phase.

During chronic pericarditis, the pattern of renal function was more variable than during the acute phase. In case 7, GFR and RPF decreased toward the control level but returned to the high level of the acute phase pre-terminally; FF increased slightly. In dogs 1 and 2A, GFR and RPF were low while FF was elevated (see Table I for evaluation of C_{CR} and C_{PAH} in dog 2A; the animal weighed 15 kg. preoperatively). It should be pointed out that an important difference existed between dog 7 and dogs 1 and 2A. Dogs 1 and 2A became depleted of protein while plasma proteins in dog 7 were never below 5.4 gm.%. Furthermore, the drop in GFR and RPF in dog 1 occurred concomitantly with the development of protein depletion.

5. *The effect of abdominal paracentesis on systemic venous pressure and renal function*

The purpose of this experiment was to determine whether the elevated venous pressure was causally related to the reduced renal function and electrolyte excretion during chronic pericarditis. Clearances of CR and PAH, Na and Cl excretion, and external jugular and femoral venous pressure were determined before, immediately following, and 1 to 2 days after removal of ascitic fluid. The changes associated with paracentesis were studied on five occasions in dog 1 and one time in each of dogs 2A, 4, and 7.

Abdominal paracentesis was consistently accompanied by a fall in external jugular and femoral venous pressure (Figures 1, 4). An alteration in renal hemodynamics occurred in only one instance; in dog 2A, GFR increased from 28 to 34 cc./min. but RPF remained unchanged. Diuresis failed to occur; Na and Cl excretion remained at a low level (1–5 μ.eq./min.). Saline loading was not used in these experiments because the dogs were loaded with large depots of salt and water; any added salt load passed almost quantitatively into the ascitic fluid. Therefore, it seems necessary to postulate that factors other than elevated venous pressure resulted in the low GFR and RPF and the salt and water retention during chronic pericarditis.

6. *Pathological findings*

The pericardial tissues showed evidence of a marked inflammatory reaction. In chronic preparations, thickening and fibrosis of the visceral and parietal pericardium were observed and the inflammatory process involved the superficial layer of the myocardium. The surface markings of the heart were com-

pletely obliterated in the region of the cellophane. Less that five cc. of pericardial fluid was removed at autopsy in any case. No instance of constriction of the superior or inferior vena cava was found. Hydrothorax was present in cases that succumbed during the acute stage and in chronic preparations whose exitus was the result of pericardial disease. Only two cases (5 and 8) showed gross evidence of pulmonary edema with a pink frothy fluid in the bronchi and trachea. Pulmonary congestion was observed only in dogs dying of acute pericarditis. In dogs with ascites, the liver and kidneys showed evidence of chronic passive congestion; on the surface of the liver a thick fibrinous exudate was present.

DISCUSSION

Sequence of events in experimental pericarditis

Following implantation of cellophane into the pericardial cavity an inflammatory reaction ensued. Fibrosis, thickening, and scarring of the parietal pericardium resulted; epicardial involvement extended into the superficial layer of the myocardium. These pathological changes and the tamponade from the cellophane resulted in an elevation in right ventricular diastolic pressure. From the available data, the sequence of changes terminating in venous hypertension cannot be outlined with certainty. However, the elevation in right ventricular diastolic pressure was accompanied by an equivalent rise in mean right auricular pressure, a decrease in the gradient from the peripheral veins to the heart, and a rise in peripheral venous pressure. Hypervolemia may have been a contributory factor to the development of venous hypertension. During the latter part of the acute phase, peripheral venous pressure declined but remained higher than the control level probably as a result of the high right ventricular diastolic pressure. The fall in venous pressure may have been related to diminution of the constrictive process as the inflammation subsided. Another possible mechanism for the decline in venous tension was the fall in plasma volume which accompanied the spontaneous diuresis. Also, the possible role of venomotor tone in the maintenance of venous pressure should be pointed out although a satisfactory method for measurement of venous tone was not available. The initial changes on the venous side of the circulation were accompanied by a decline in arterial pressure and the development of a "paradoxical pulse." As the inflammatory reaction subsided arterial pressure returned to the control level but the "paradoxical" nature of the pulse remained. These findings are in agreement with more extensive studies of cardiovascular hemodynamics in experimental pericarditis by Isaacs (39).

During the chronic phase, the accumulation of ascitic fluid was accompanied by a further elevation in external jugular and femoral venous pressure; abdominal paracentesis resulted in a fall in venous tension to the level observed at the end of the acute phase. The response of the systemic veins to the pres-

sure exerted by the ascitic fluid may have resembled the response of a physical fluid system to local pressure; the effect of increased intra-abdominal pressure from the ascites may have been transmitted uniformly throughout the systemic veins. This explanation would account for the rise in venous tension as ascites developed and the immediate fall following paracentesis.

Other workers (17, 20, 39) have measured cardiac output in dogs with experimental pericarditis. Fishman and associates (17) were unable to detect a significant change in resting cardiac output until pre-terminally in preparations made by enveloping the heart with polythene. On the other hand, Isaacs (39) measured cardiac output daily during acute pericarditis and found an elevation during the first 5 or 6 postoperative days. Although these results appear conflicting, their divergence may be related to the difference in the preparations.

In chronic experimental pericarditis, Beck (20) was first to indicate that cardiac output is reduced. The most extensive data have been presented by Isaacs (39) who found a progressive decline in cardiac output during observations over a period of several months. The chronic preparations in the present study resembled those of Beck and of Isaacs in which the irritative material covered the right heart or entire organ. It may be concluded that the basic cardiac defect in chronic experimental pericarditis involving the right or entire heart is the same as that reported in studies of chronic constrictive pericarditis in man (42–45).

The relation of GFR and RPF to changes in other functions during the first three or four postoperative days was not determined because clearance studies were not conducted until fever subsided. Later during the acute phase, renal function was elevated during the acute depressor response in arterial pressure and during maximal hemodilution. Chronically, the decline in renal function seemed to be most closely related to protein depletion.

The onset of salt and water retention occurred before or concomitant with changes in cardiovascular hemodynamics. Edema appeared on the first to fourth postoperative days. Plasma volume, as indicated by changes in hemoglobin, hematocrit and T-1824 dye space increased concurrently with salt and water retention and declined during the diuresis terminating the acute phase; chronically T-1824 dye space was elevated. Initiation of chronic fluid retention was accompanied by the development of ascites. In all cases, ascites formation was preceded by a systemic venous pressure greater than 160 mm. of water. Whether ascites preceded or succeeded the initiation of salt and water retention by the kidney cannot be answered definitely.

Possible mechanisms for alterations in renal function

Available data have not provided an adequate explanation for the elevation in GFR and RPF. Consideration of the relation of increased renal func-

tion to physiologic changes known to alter the renal circulation suggests several possible mechanisms. These include (1) increased cardiac output, (2) renal hyperemia as a part of a generalized decrease in peripheral resistance which resulted in a drop in arterial pressure, (3) changes associated with expansion of the extracellular fluid volume, and (4) direct action of a humoral agent on the renal arterioles.

The relation of changes in cardiac output to increased renal function cannot be determined from available evidence. Cardiac output was not measured in the present study and the results from other studies of acute pericarditis (17, 39) appear conflicting. For a satisfactory evaluation of this relationship, simultaneous measurements of these functions should be made. The second mechanism was suggested by Stamler and associates (46) as an explanation for the renal hyperemia accompanying acute sterile abscess formation in dogs. The occurrence of increased renal function during the depressor response of acute pericarditis and the close negative correlation between the changes in these functions during the acute and pre-terminal phases of case 7 indicates that this mechanism was also operative in experimental pericarditis. The same relation was observed for changes in renal function and the volume of extracellular fluid. Alterations in the volume of extracellular fluid were indicated by changes in Na, Cl, and water balances and body weight. Therefore, another plausible mechanism is to be found in changes associated with an expanded extracellular fluid volume. Finally, the possibility of the direct action of a humoral agent on the renal arterioles cannot be excluded.

The decline in renal function during the chronic stage in dogs 1 and 2A seems explicable on the basis of protein depletion. Both dogs were markedly protein depleted and showed a low renal function. In dog 1, the decline in GFR and RPF occurred concomitant with protein depletion. More convincing evidence of this relationship has been obtained from the study of dogs with constriction of the thoracic inferior vena cava (47). These dogs also showed a decline in renal function concomitant with protein depletion; the changes were reversible with a high protein, low salt diet.

Other factors such as decreased cardiac output and elevated venous pressure must be considered. As pointed out previously, Isaacs (39) has shown that cardiac output is markedly depressed in chronic pericarditis with ascites. However, the elevated GFR and RPF in case 7 in which the plasma proteins were normal may indicate that low cardiac output was not causally related to the alteration in renal function. Also, it does not appear that venous hypertension altered the renal circulation; marked drops in venous pressure were unaccompanied by a rise in GFR and RPF. Regardless of the mechanisms involved, dogs with chronic experimental pericarditis and protein depletion afforded the opportunity for evaluation of the role of various factors in the

retention of salt and water by a kidney with a renal functional pattern identical with the patient with congestive heart failure.

Mechanisms of fluid and electrolyte retention

Elevated venous pressure. The role of venous hypertension in the pathogenesis of edema has been a subject of considerable discussion for many years. It seems established that an elevation in capillary pressure secondary to venous hypertension favors extravasation of fluid from the capillaries into the surrounding tissue spaces (11). Disagreement has arisen in regard to the changes initiating salt and water retention in such syndromes as congestive heart failure. Whatever the initial change, it seems clear that the kidney must retain salt and water for a significant amount of edema and ascites to develop. Otherwise, the filling of a large extracellular depot with fluid iso-osmotic with plasma would lead to a marked decrease in plasma volume. Therefore, one major aspect of the problem is concerned with the effect of venous hypertension (direct or indirect) on the kidneys.

During acute pericarditis retention of salt and water by the kidney was discernible on the first postoperative day regardless of the level of venous pressure. Alterations attributable to the surgical procedure were superimposed upon the initial changes in pericarditis so that a satisfactory evaluation could not be made. Consequently, it cannot be concluded that venous hypertension initiated fluid and electrolyte retention as Fishman and associates (17) have reported. However, a high venous pressure cannot be excluded as a contributory factor to the maintenance of positive balances during the acute phase. The highest venous pressure was observed in dog 7 in which fluid and electrolyte accumulation was excessive and anasarca developed. Whether the effect of venous hypertension was limited to localization of edema fluid cannot be answered from available data.

The role of elevated venous pressure in the pathogenesis of ascites and chronic fluid retention has been indicated previously in connection with the sequence of events in pericarditis. The results of this study and other reports (20, 21) suggest that initiation of ascites in experimental pericarditis was related to the development of a critical level of systemic venous pressure of 150–170 mm. water. Recent studies (9, 16) in normal anesthetized dogs have suggested that an acute elevation of renal venous pressure resulted in a direct effect on the kidney and salt and water retention. In chronic pericarditis, a direct renal action cannot be completely excluded, however, the available evidence is more consistent with an indirect effect. Measurements of renal function before and after abdominal paracentesis failed to indicate that elevated venous pressure exerted a direct influence on the kidney. Furthermore, others (48, 49) have not observed fluid retention in the presence of a

chronically elevated renal venous pressure. Hwang and coworkers (48) constricted the abdominal inferior vena cava above the renal veins; salt and water retention did not result. Volwiler and associates (49) reported that preparations with constriction of the abdominal inferior vena cava and hepatic portal vein failed to develop spontaneous ascites but a thin watery ascitic fluid formed after large saline infusions. On the other hand, constriction of the inferior vena cava above the entrance of the hepatic vein (47, 50, 51) resulted in large quantities of spontaneous ascites. Volwiler (49) suggested that hepatic congestion leads to dilation of the lymphatics of the liver and extravasation of lymph into the peritoneal cavity. The high protein content of the ascitic fluid found in this study and by McKee and associates (51) and others (47) in dogs with thoracic inferior vena cava constriction supports this hypothesis. Further evidence for this view was presented in the recent report of Nix and coworkers (52) that hepatic lymph flow was increased several fold following thoracic inferior vena cava constriction. Therefore, it appears that the effect of venous hypertension on ascites formation was indirect; elevated venous pressure localized a depot of extracellular fluid in the peritoneal cavity. Other factors must be considered to explain the salt and water retention associated with the accumulation of ascites.

Low glomerular filtration rate. Several workers (9, 15, 16, 18, 53) have demonstrated that an acute reduction in the rate of glomerular filtration was accompanied by more complete tubular reabsorption of Na and water. The decrease in GFR resulted from a fall in arterial pressure or rise in renal venous tension in normal anesthetized dogs or was associated with dehydration in dogs with diabetes insipidus. In the present study, extensive observations were made in order to evaluate this mechanism.

During acute pericarditis and the chronic phase of pericarditis in dog 7, GFR was elevated. These results demonstrate that factors other than a reduction in the rate of glomerular filtration were responsible for salt and water retention during these observations. On the other hand, when GFR was low in dogs with protein depletion, this mechanism must be considered. In dogs 1 and 2A in which the most marked drops in venous pressure occurred following paracentesis, the low rate of glomerular filtration cannot be excluded as a possible mechanism for the continued retention of fluid and electrolytes. It should be pointed out, however, that homeostatic mechanisms can establish Na equilibrium in the presence of a low GFR. This has been demonstrated in hypophysectomized dogs (54, 55). It may be concluded that available data are insufficient to demonstrate a causative relation between a low rate of glomerular filtration and salt and water retention in experimental pericarditis.

Altered adrenocortical activity. It is evident from the foregoing discussion that factors other than elevated venous pressure and low GFR must be sought to

explain the salt and water retention in acute pericarditis. The striking qualitative resemblance in N and electrolyte balances between the sham operated dogs and preparations with acute pericarditis suggests that the same mechanism was operative in both instances. The pattern of negative N and K and positive Na and Cl balances following surgery seems well established (56–60). Selye (61) suggested that these changes are the result of adrenal cortical stimulation. Evidence for adrenocortical hyperfunction following surgery includes (1) decline in eosinophils immediately postoperatively (62) and failure of eosinopenia to occur following adequate stimulation in adrenalectomized animals (63), (2) increased urinary excretions of corticoids (64, 65), and (3) occurrence of a postoperative syndrome with K deficit and metabolic alkalosis resembling some patients with Cushing's syndrome (60).

Of importance in relating changes in electrolyte balances to altered adrenocortical activity is the finding of a low Na, high K pattern of fecal electrolyte excretion in both acute and chronic pericarditis. Several years ago, Dennis and Wood (66) showed that adrenal cortical hormones regulate Na and K transfer across the wall of the gut. After hormone withdrawal, Na reabsorption decreased or movement reversed while K was reabsorbed more slowly; these changes were reversible with hormone administration. More recently, Berger and associates (67) reported that the administration of DOCA in rats and man was accompanied by a reduction in fecal Na excretion. Of further interest is the low Na concentration of sweat in cardiac failure (12), cirrhosis of liver (8), and Cushing's syndrome (68). A low Na and high K concentration in saliva has been reported for patients with congestive heart failure (69) and cirrhosis of liver (8). It appears, therefore, that the pattern of fecal electrolyte excretion in experimental pericarditis may indicate hyperfunction of the adrenal cortex in regard to the action of Na retaining hormones.

Consequently, the results of this study and other previously cited evidence indicate that altered adrenal cortical function and elevated venous pressure were two of the most important factors in the pathogenesis of edema and ascites in experimental pericarditis. The role of venous hypertension may have been limited to the localization of a depot of extracellular fluid as edema or ascites. Movement of electrolytes and water from plasma to expand these extracellular depots was accompanied by salt and water retention by the kidney. Hyperfunction of the adrenal cortex with increased output of DOCA-like hormones might account for the more complete reabsorption of salt and water by the renal tubules. If passage of water and electrolytes from plasma to ascitic fluid stimulated the adrenal cortex, a volume or electrolyte concentration receptor capable of increasing the output of salt retaining hormones by the adrenal cortex is implied. However, support for this hypothesis from studies of plasma volume and electrolyte concentration is lacking. In this connection,

Lombardo and associates (70) have postulated that a receptor in the cranium is capable of responding to removal of small amounts of blood and effecting a decrease in the renal excretion of Na. More convincing evidence for the existence of a receptor-effector system is needed as well as information in regard to its mechanism of action.

SUMMARY AND CONCLUSIONS

(1) Experimental pericarditis was produced by implantation of irritative cellophane into the pericardial cavity of 13 dogs.

(2) The experimental period was represented by two phases of fluid and electrolyte retention. The acute phase lasted from 10 to 12 days and was characterized by the formation of edema. During the chronic stage, ascites was the principal depot for storage of electrolytes and water. This phase lasted as long as six months.

(3) Na, Cl, and water balances were markedly positive during both phases of pericarditis. Salt and water retention was accompanied by a decrease in hemoglobin and hematocrit and an elevation in T-1824 dye space. K balance was negative for the first day or two postoperatively; in the presence of ascites K balance was slightly positive. N balance was negative for the first 4 to 8 days of acute pericarditis and in the presence of extensive ascites.

(4) GFR and RPF were elevated during acute pericarditis. During the chronic phase, renal function returned to the control level or remained elevated unless protein depletion occurred. In this event, GFR and RPF decreased while FF increased.

(5) No correlation was observed between the level of GFR and salt and water retention.

(6) Systemic venous, right auricular and right ventricular diastolic pressure were elevated during acute and chronic pericarditis. An arterial depressor response occurred during acute pericarditis but chronically arterial pressure was maintained until pre-terminally.

(7) The relation of venous hypertension to the onset of fluid and electrolyte retention during acute pericarditis could not be determined because of the effect attributable to the surgical procedure. Later during the experimental period, the occurrence of a spontaneous diuresis in the presence of a high venous pressure and failure of a diuresis to occur with a marked fall in venous tension may indicate that other factors were more directly related than venous hypertension to the retention of salt and water.

(8) The close similarity in the pattern of electrolyte and N balances between the sham operated dogs and preparations with acute pericarditis suggests hyperfunction of the adrenal cortex.

(9) The low Na, high K pattern of fecal electrolyte excretion during both

phases of pericarditis may also be an indication of altered adrenocortical activity.

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CONSTRICTIVE ENDOCARDITIS

Report of a Case

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In 1936 Loeffler (1) described two cases of "parietal fibroplastic endocarditis" in adults. The endocardium of both ventricles was involved extensively. The clinical picture was that of chronic constrictive pericarditis. Loeffler believed that blood eosinophilia was an invariable feature of the active stages of the disease but might disappear later. His patients were afebrile.

The following case resembles in most respects the condition described by Loeffler. Constrictive pericarditis was thought to be present but a perfectly delicate pericardium was found at operation. Because of the close similarity of the clinical manifestations (and probably of the pathological physiology) to those of constrictive pericarditis, the authors prefer the term "constrictive endocarditis."

CASE REPORT

Clinical history: M. L. (J.H.H. 111821), a white female patient of German extraction, was born in 1890. Symptoms had their onset in 1933 with pain located in the sides of the neck and radiating down the arm, first on one side, then on the other. Somewhat later burning substernal pain, malaise, and easy fatigability appeared and were followed by progressive peripheral edema and ascites. Dyspnea was a relatively inconspicuous feature. In the past there had been no rheumatic fever or any illness of consequence. There was no history of dietary inadequacy or excessive consumption of alcohol.

When she was first admitted to the Johns Hopkins Hospital in March, 1936 the principal findings were marked venous engorgement with slight inspiratory filling of the neck veins, blood pressure between 98/84 and 114/86 mm. Hg., enlarged liver and spleen, and massive ascites and peripheral edema. She was thought to be cyanotic. Venous pressure was 300 mm. saline. EKG's showed low voltage of the QRS complexes and low or slightly inverted T waves in all three limb leads. The serologic test for syphilis and skin tests with old tuberculin 1:100 were negative. By x-ray the heart was triangular in contour but within normal limits for size. Esophagogram revealed no left auricular enlargement. Pulsations of the heart border were said to have been normal fluoroscopically. Means of kymographic studies were not then available. Digitalis did not reduce the venous pressure or help the patient symptomatically. Furthermore, it appeared to have precipitated auricular fibrillation.

Exploration by Dr. William F. Rienhoff, Jr., on May 27, 1936, revealed that the right auricle was abnormally large and tensely distended but the pericardium was normally delicate with no adhesions. No thrills were palpable.

The patient was essentially afebrile during the entirety of her long period of observation. The pronounced ascites and leg edema continued; at least thirty abdominal paracenteses were performed in the last eighteen months of life. In the last few days of life the patient developed wheezing respiration with prolonged expiratory phase and died on September 15, 1937.

Table I lists some of the hematologic findings during the course of her illness.

TABLE I

DATE	W.B.C.	% EOSINOPHILES	SEDIMENTATION RATE	HGB. (GM.) %
			mm.	*gm. %*
3-24-36	11,120	0	—	—
4-6-36	6,600	0	—	102
4-15-36	5,600	1%	6.5	—
4-23-36	6,000	—	11	—
5-4-36	5,600	1%	3	92
6-19-36	9,200	—	21	—
7-28-36	8,360	0	—	88
12-16-36	6,560	7.5%	5	92
1-14-37	7,800	3%	—	94
7-18-37	8,300	1%	—	98
8-5-37	9,650	0	—	98

Postmortem findings: The autopsy (No. 15494) was performed within two hours of death. The external examination revealed a well-nourished body weighing 69 kilograms and measuring 160 cms. in length. There was slight edema of both ankles and the dependent portions of the body. There were several small paracentesis scars and a healed thoracotomy incision. Fibrous pericarditis which had not been present at the time of previous surgery was noted. The pleural cavities were free of fluid or adhesions. The lungs showed no edema, congestion, or iron-staining macrophages. There was an extensive purulent bronchitis with minimal lobular pneumonia.

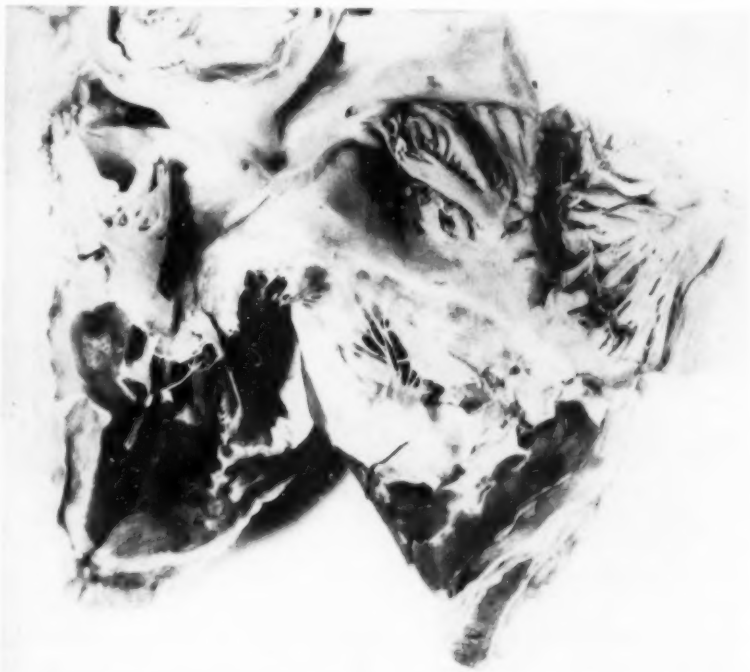
The peritoneal cavity contained 600 cc. of dark yellow fluid and both the spleen and liver were enlarged. The liver weighed 1750 grams and showed scarring which microscopically was centro-lobular in distribution. Other areas showed the characteristic "nutmeg" effect of chronic passive congestion. The spleen weighed 280 grams and showed the gross and microscopic changes of chronic passive congestion. The pancreas showed acinar atrophy characteristic of chronic passive congestion. The kidneys showed scattered cortical scars. The adrenals were normal as were the other abdominal and pelvic organs.

The most striking findings were in the heart (Fig. 1), which weighed 560 grams. The post-operative fibrous pericarditis has been mentioned. *The ventricles were not dilated or hypertrophied*, although the walls of both auricles were somewhat thickened. *The endocardial surfaces of both ventricles were markedly thickened by a layer of fibrous tissue* which measured up to 4 mm. in greatest thickness. Only the surfaces of the interventricular septum were spared. The

FIG. 1. A. Left heart. There is a dense pearly thickening of the endocardium without involvement of the valve leaflets.

chordae tendineae appeared shortened but the valve leaflets were all delicate. There was no endocardial scarring in either auricle. The coronary arteries were carefully examined and showed no arteriosclerosis or occlusion. Microscopic sections (Fig. 2) of the ventricle showed a dense fibrous layer beneath the endocardium and a looser layer of chronic granulation tissue between this and the myocardium. The dense inner layer showed relatively acellular hyaline areas

intermingled with areas of fibrous tissue. In these hyaline areas elastic fibrils were demonstrated, arranged at times in an orderly, parallel fashion, at times in a haphazard, fragmented manner. The dense innermost layer gradually blended into a zone comprised of abundant new vessel formation with diffuse and perivascular infiltrations of lymphocytes, monocytes, and occasional plasma cells. No eosinophiles were seen in the tissues. The myofibrils blended with this granulation tissue layer, which formed deep projections around the thebesian vessels. The thebesian channels were very prominent. The myo-



B. Right heart. The same change is seen. The sparing of the septum is particularly well demonstrated.

cardium showed only a rare focal scar and no inflammatory infiltrate other than the perivascular infiltrate along the deep endocardial projections. A section through the ventricular septum showed no endocardial thickening but many hypertrophied muscle fibers.

The thyroid showed some scarring with lymphocytic infiltration. The brain and spinal cord were not examined.

Anatomical diagnosis: Extreme scarring of endocardium of right and left ventricles. Chronic passive congestion of liver, spleen, and pancreas. Adhesive

pericarditis and mediastinitis following pericardiotomy. Purulent bronchitis and minimal lobular pneumonia. Scarring and lymphocytic infiltration of thyroid.

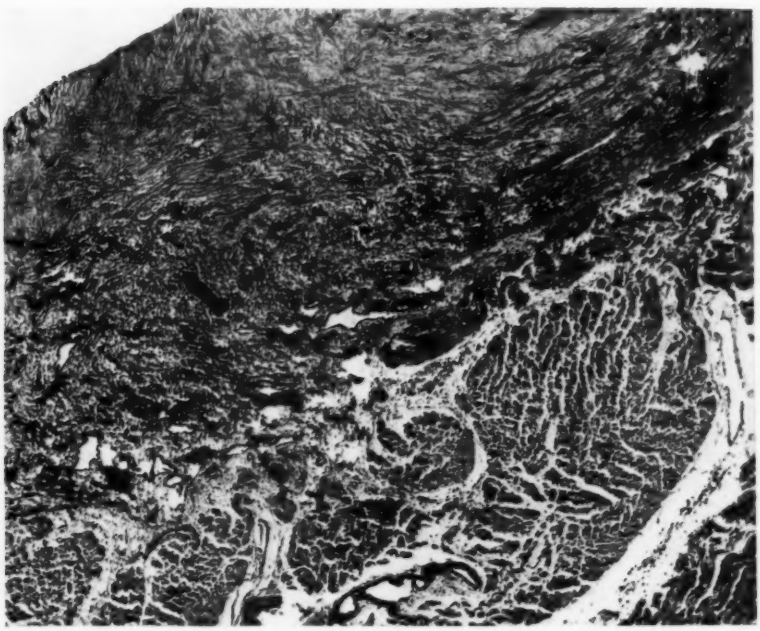


FIG. 2. Photomicrograph of right ventricle showing marked fibrous thickening of the endocardium. The fibrous layer is separated from the myocardium by a zone of inflammation and new vessel formation. There are conspicuous thebesian channels.

DISCUSSION

Clinical features: At the age of 43 years this white female patient developed persistent ascites and edema with which she died four years later. The heart except for the right auricle was normal in size. There was no apparent reason for the chronic congestive failure. Venous pressure was persistently elevated during an 18 month period of close observation. Autopsy revealed dense endocardial fibrosis in both ventricles as the only explanation for the clinical picture.

Berblinger (2) reviews 10 cases of fibroplastic parietal endocarditis from the literature and adds one of his own. In most respects the clinical picture in those cases which had right ventricular involvement with or without involvement of the left ventricle was the same as that in the case reported here. The cases which most closely resembled ours clinically and pathologically were those of Loeffler (1) (first case), Mumme (3), Fossel (4) (first case), and Egger (5). All

of these patients had a syndrome indistinguishable from that of constrictive pericarditis. In these cases dyspnea was a relatively inconspicuous feature. Dyspnea and pulmonary edema was the main feature of those cases with sole or predominant involvement in the left ventricle, e.g., Berblinger's own case (2).

Leoffler (1) emphasized eosinophilia as an important feature of these cases. In the eleven cases collected by Berblinger (2) differential white counts are reported in nine. Of these, seven had eosinophilia. The highest eosinophile count in our patient was 492 per cu. mm. (7.5%). Absolute eosinophile counts as high as 18,522 per cu. mm. have been described (3) in this condition. Loeffler (6) presented suggestive evidence that the presence or absence of significant eosinophilia is dependent on the stage of the disease in which the patient is observed. The absence of eosinophilia in our case may have been due to the fact that the patient was observed first almost three years after the onset of her disease.

Fever was absent in this patient and has not been present in the previously reported cases.

The predominant physiologic defect in this patient was quite clearly an impediment to diastolic filling of the ventricle. In constrictive pericarditis this same defect is probably responsible for the characteristic findings on roentgenkymography and electrokymography (7), on cardiac catheterization (8), and on ballistocardiography (9). Whether these same characteristic changes will be present in constrictive endocarditis awaits the study of such a patient by these newer techniques.

Given the clinical picture presented by this patient, the diagnosis of constrictive endocarditis can be strongly suspected under the following circumstances:

1) Exclusion of pericardial involvement by thoracotomy or intrapericardial injection of air;

2) lack of evidence for any of the valvular or extracardiac causes of failure;

3) normal sized heart (ventricles).

Pathological features: The striking endocardial fibrosis of both ventricles resembles at least superficially that seen in endocardial fibroelastosis (10) (11) of infants. However, the late onset of symptoms and the obvious presence of chronic inflammatory changes in association with the fibrous endocardial thickening suggest that the analogy extends only to the site of the lesion and the effect on the circulation.

It is clear that the process in the authors' case was basically one of fibrous thickening of the endocardium. The diffuseness with involvement of both ventricles makes it quite unlikely that organization of endocardial thrombi is the basic or predominant mechanism.

Occasional cases of longstanding Fiedler's myocarditis (12, 13) show areas

of endocardial thickening. Although the present case is distinguished by the absence of myocardial inflammation or scarring as well as by the absence of tissue eosinophilia, the possibility that this lesion may be the end result of an unusual form of such isolated endo-myocarditis cannot be excluded.

Etiologic considerations: At the outset it must be stated that there is no worthwhile evidence for any one of the etiologies which have been proposed. Loeffler (7) believes this condition to be in the "rheumatic symptom complex." Several of the cases (1, 2, 3, 14) have had thickening of the mitral or tricuspid valves. There is no evidence that this is more than a secondary involvement by the process which is involving predominantly the parietal endocardium. The cases have shown no definite clinical or pathological stigmata of rheumatism.

Smith and Furth (15) suggest that this process may be on a nutritional basis. It is not certain that they were discussing the same condition as that from which this patient suffered. Evidence even for a malnutrition etiology of the condition they described is lacking. In the somewhat similar endocardial fibrosis which occurs in African natives, Davies (16) suggested, without supporting evidence, a nutritional etiology. The disease has been observed in Englishmen residing in Africa (19).

Endo-myocardial lesions have been produced in experimental animals with various viruses (17). The pertinence of such experiments to the clinical state discussed here is not established.

SUMMARY

A case of chronic constrictive endocarditis or parietal fibroplastic endocarditis is presented. The clinical picture was precisely that of chronic constrictive pericarditis. The diagnosis may be suspected clinically if the heart is not enlarged, if pericardial disease has been excluded, and if there is nothing pointing to the other causes of heart failure. The etiology is unknown.

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HYPERGLYCEMIA AND ITS RELATIONSHIP TO DIABETIC RETINITIS AND GLOMERULAR NODULES*

A Preliminary Report

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An analysis of 190 patients with diabetes mellitus autopsied at the Johns Hopkins Hospital has shown that those patients with glomerular nodules of the Kimmelstiel-Wilson type rarely accumulate ketone bodies in sufficient degree to develop acidosis (1). The method used in this study consisted of a survey of the patients' charts which was independent of the examination of the kidneys by the pathologist.

Further study of the data on which these observations were based reveals that of 51 patients with glomerular nodules, 45 were noted clinically to have aneurysms of the retinal capillaries. Retinal aneurysms occurred rarely without concomitant glomerular nodules. Of 56 patients with such aneurysms only 3 gave a history of acidosis. Of the 45 patients with a combination of retinal aneurysms and glomerular nodules, there was no instance of diabetic acidosis. It seems apparent that there existed in this group a type of diabetes mellitus characterized by hyperglycemia without acidosis in which there was a common and perhaps exclusive occurrence of retinal aneurysms and glomerular nodules.

The inability of these patients to accumulate ketone bodies even under severe stress led to the conclusion that they have a supply of oxalacetate (2) adequate to remove promptly the products of fat metabolism, and that, therefore, these patients have sufficient endogenous insulin to metabolize glucose.

It was reasoned that patients with retinal aneurysms and hyperglycemia would not develop diabetic acidosis when their daily insulin was withheld. A study was made of five patients with retinal aneurysms, fasting blood sugar concentrations in excess of 200 mgm% and a daily insulin dosage of 15–30 units. When insulin was discontinued for three weeks, none of these patients developed a positive test for acetone or diacetic acid in the urine. Since the insulin dosage in these patients was not large, a patient (P. B.), with a twelve-year history of glycosuria, whose hyperglycemia was uncontrolled in spite of 50 to 130 units of insulin daily, and who had capillary aneurysms of the retina was admitted to the hospital for study. He was given a diet of P 140 grams F 130 grams C 270 grams and 55 units of PZI daily. This resulted in a fasting blood sugar of 120–150 mgm%. Insulin was then withheld for 30 days and the urine examined four times daily for acetone and diacetic acid. No ketone bodies

*Presented at the Johns Hopkins Medical Society, January 14, 1952.

were found during the study period, in spite of the development of a skin abscess and fever approximately two weeks after stopping insulin. After three weeks without insulin he was put on a high fat diet (P 100 grams, F 200 grams, C 125 grams) for four days without developing ketonuria or change in carbon dioxide combining power of the blood.

These preliminary clinical results strengthen the conclusion derived from the analysis of the pathological material that patients with capillary aneurysms of the retina have hyperglycemia but do not require exogenous insulin to prevent the accumulation of ketone bodies. It is our postulate that the hyperglycemia without acidosis in this group of patients has a different mechanism than simple insulin deficiency. Relative excess of hyperglycemia—glycogenolytic hormone from the islets of the pancreas (3) could explain the presence of hyperglycemia without acidosis, in this group of patients.

SUMMARY

The suggestion is made that patients with capillary aneurysms of the retina, glomerular nodules and hyperglycemia without acidosis have a specific metabolic defect. Studies are in progress on the exact nature of this metabolic defect and its role in the genesis of the retinal and renal capillary disease.

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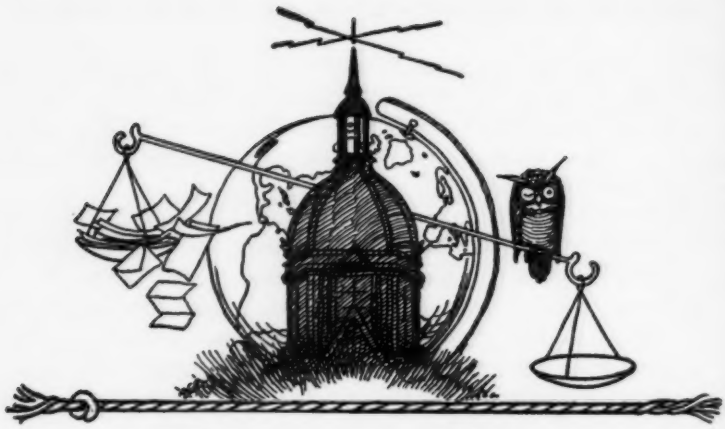

BOOK REVIEWS

(These reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of the Bulletin)

A History of Neurological Surgery. Edited by A. EARL WALKER. 583 pp., $12.00. *The Williams & Wilkins Co., Baltimore, Md.*

Successful operations upon the nervous system have now been an established fact for a number of decades, and the special application of surgery to the brain, spine, peripheral nerves and autonomic system has long been recognised as the unique function of the neurologic surgeon. At long last we are presented with an adequate and well-documented story of the development of this surgical specialty. Dr. Walker and his associates have performed a real task which has been crying for completion for many years. Surrounded as it has been by legend, myth and superstition, the story of the development of surgery of the nervous system has never before been adequately presented. The complexities of the problem and the need for almost infinite patience in attempting to interpret in their proper light the hundreds and thousands of details made the job seem beyond human capacity. Nevertheless, it has been done.

Eleven of Walker's associates participated in production of the work, which is an outcome of divisional seminars devoted to the discussion of the development of surgery of the nervous system. One might think that the multiplicity of contributors would make for loss of continuity in a history, but this is dexterously avoided by dividing the volume into chapters which deal individually with the various branches of neurological surgery, from diagnostic procedures to consideration of surgical therapy of pathology in each subdivision of the nervous system. Thus each chapter is more or less autonomous. The reader interested for the time being primarily in pituitary surgery or lesions of the posterior fossa is not led far afield by a discussion of craniocerebral trauma, vascular anomalies or schizophrenia.

Adequate consideration is given the newer aspects of neurological surgery—the treatment of epilepsy, motor disorders and the surgery for pain. The history of the last has admittedly just begun, and the authors express confidence that pharmacologic rather than surgical procedures will supply the solution to what is at present still a distressing problem.

As an introduction to each chapter there is a brief biographical sketch of one of the out-

standing surgeons who contributed to the advance of surgery of the nervous system. This not only helps in temporal orientation but emphasizes how much has been done by so few. All in all, the book satisfies a great need and should be read with interest and profit not only by all students of neurological surgery, but by every student of medicine, as well.

F. J. O.

Clinical Pediatric Urology. By MEREDITH CAMPBELL. 1113 pp., $18.00. *W. B. Saunders Co., Philadelphia, Pa.*

This is *the* definitive text on urological principles and practice concerning infants and children. The fact that it is the only significant treatise on the subject makes its excellence all the more gratifying.

The author, who is widely known for his previous (now out of print) two-volume work on pediatric urology and for numerous contributions to the pediatric and urological literature, has in a single beautiful volume presented an up-to-date encyclopedic, authoritative and valuable book of the first rank. There are fourteen chapters encompassing: methods of examination and diagnosis, urinary obstructions, embryology and anomalies of the urogenital tract, urinary infections, the male genital tract and female urethra, urogenital injuries, urinary calculus disease, tumors of the urogenital tract, the adrenals, neuromuscular uropathy, enuresis, and operative procedures. The brief but pointed chapter on urologic surgery is enhanced by an excellent section on nursing care written by Helen T. Goddard, R. N. The final chapter on nephritis and allied diseases in infancy and childhood has been clearly and succinctly written by Elvira Goettsch, M.D. and John D. Lyttle, M.D., with the wisdom and authority of long clinical pediatric experience.

The book has no major faults. Throughout, it is handsomely and appropriately illustrated. The reproductions of x-rays are of particularly good quality, and the author's use of a "schema" to represent his interpretation of the x-rays and of complicated autopsy specimens is very lucid and helpful. Like the photographs of gross pathology, the photomicrographs are beautifully clear (e.g. the section of Wilms' tumor) and match the concise text. The sections on embryology and on operative procedures are especially well illustrated. It is gratifying to find so much important material so well organized and presented in a single volume. The sections on rapidly changing fields like antibiotics and adrenal steroids are very much up-to-date. He makes good use of didactic classifications without losing the reader's interest. The attention to detail, as in drug and radiation dosages and descriptions of operative techniques and preoperative and postoperative care is bound to be extremely useful to the reader in search of the exact technique involved.

One of the best features of the book is the complete and up-to-date bibliography of *useful* contributions in the literature at the end of each chapter. He frequently makes valuable cross references in the text to other sections of the book containing important related facts. The index is complete.

The book is a vast, orderly, and easily entered storehouse of available knowledge concerning pediatric urology. The author writes clearly and directly of his own extensive experiences. Throughout the book the reader has the feeling of authority, wisdom, care and interest on the part of the author. He knows his subject, loves children and wishes to share his knowledge and experience for their benefit. This is bound to be a treasured reference book of facts and figures on common conditions as well as the unusual, rare and bizarre. Most readers, having seen a case or two of this or that oddity, will be interested and amazed to find several cases reported, usually from Campbell's own experience, as well as the pertinent literature on each subject.

The book is certain to be indispensable to students, pediatricians, and especially urolo-

gists. It will be useful both as a reference and as a text, for all physicians who deal with children.

W. E. G.

A Color Atlas of Morphologic Hematology. By GENEVA A. DALAND. Edited by THOMAS HALE HAM. Illustrations by ETTA PIOTTI. 74 pp., $5.00. *Harvard University Press, Cambridge, Mass.*

This small atlas was designed to be used as a companion volume to *A Syllabus of Laboratory Examinations in Clinical Diagnosis*, another recent product of the Thorndike Laboratory. Techniques for examining the blood have been described in the Syllabus, while the Atlas is limited essentially to descriptions of the blood as seen in films stained with Wright's stain. The histogenesis of the blood is outlined diagramatically to portray the maturation of the several series of blood cells. Normal and abnormal blood patterns are illustrated by 14 colored plates. These plates are reproductions of camera lucida drawings painted in water colors. They provide reasonably good representations of normal and abnormal blood cells. There are no illustrations or descriptions of bone marrow.

The Atlas should be an adequate teaching aid for the student or laboratory technician. The author might profitably have called attention to the fact that apparently minor abnormalities of the blood may be significant and that the physician is often called upon to arrive at a diagnosis long before blood abnormalities have reached the degree portrayed in the illustrations. Physicians troubled by the possibility of accidental transmission of hepatitis will be distressed by the method recommended for sterilization of blood lancets.

C. L. C.

Leitfaden Der Laparoskopie Und Gastroskopie. By H. KALK and W. W. BRUHL. 158 pp., Ganzleinen DM 27.—*George Thieme Verlag, Stuttgart, Germany.*

This manual of Peritoneoscopy and Gastroscopy has been written by H. Kalk, Professor of Internal Medicine at the City Hospital, Kassel, who is one of the pioneers in peritoneoscopy, and by W. Bruhl of Arolsen, who is the physician-in-chief of the Paulinen-hospital in that city. Both are physicians practicing internal medicine.

The book is written in German and contains many excellent illustrations in both color and black and white. It is unfortunate that these illustrations are not of more varied pathological lesions, so that it could serve as a diagnostic atlas. For instance, many different phases of hepatitis and cirrhosis of the liver are shown, but there is no picture of tuberculous peritonitis or malignant metastases, each of which has a rather characteristic appearance. The same criticism is true of the illustrations for gastroscopy.

The instruments used for peritoneoscopy in Germany are described in detail, along with the technic of their use. Unfortunately, the Ruddock peritoneoscope which is the standard in this country is not included. Since this instrument differs in both its construction and technic for use from those described, the manual would be of little help to an American peritoneoscopist. It is interesting to note that the German instruments are not equipped with a visual biopsy forceps, as is the Ruddock peritoneoscope, and their biopsies are obtained by inserting an aspirating needle through another puncture wound and guiding it by, observation through the peritoneoscope, into the liver substance. This requires a second puncture into the abdominal wall.

Kalk mentions that the book is based upon his personal experience with over 2000 peritoneoscopic examinations. It would have added much to the value of the book if these could have been tabulated as to findings, percentage of accuracy, complications, etc. It is

possible, indeed probable, that destruction of case records during the war may have made this impossible.

These criticisms apply equally to the section on gastroscopy.

In conclusion, this manual is not as valuable to an American beginner in either peritoneoscopy or gastroscopy as are the various articles published by Ruddock and others in the English literature. It is, however, a good book to have in the library of one who is primarily interested and experienced in those procedures. Best of all, it is heartwarming to know that Prof. Kalk is continuing his interest in a field in which he has contributed so much and to know that he survived the war. This critic eagerly looks forward to future communications from his able pen.

R. T. S.

Clinical and Roentgenologic Evaluation of the Pelvis in Obstetrics. (American Monograph Series). By HOWARD C. MOLOY. 119 pp., $2.50. *W. B. Saunders Co., Philadelphia, Pa.*

Dr. Moloy has done a very useful service in bringing together his vast experience with the science of pelvimetry and its relationship to labor and delivery. With the late Dr. Caldwell, he pioneered the concept that the architecture of the pelvis, that is its form, plays a very decided role. Previous to this significant contribution, the obstetrician dealt in terms of the size of the diagonal conjugate and the centimeters between the tuber ischii. Now all well trained obstetricians think in terms of pelvic planes and contours.

The book is well written and excellently illustrated. It is perhaps too complex to be of real value to the medical student, but it can be read with great profit by the specialist in midwifery.

It is impossible for one obstetrician to read another's book without uncovering minor differences. The reviewer feels that manually dilating the pelvic floor pre-delivery is ill advised, and also that the bare statement, "fetal embarrassment is a positive indication for termination of the labor," is dangerous. In such naked form it may condone radical procedures in the hands of the novitiate.

A. F. G.

BOOKS RECEIVED FOR REVIEW

Atelektasen der Lunge. By HANNS ALEXANDER. 58 pp., Kartoniert DM 8.70. *Georg Thieme Verlag, Stuttgart, Germany.*

An Atlas of Normal Radiographic Anatomy. By ISADORE MESCHAN. 593 pp., $ 15.00 *W. B. Saunders Co., Philadelphia, Pa.*

Autopsy Diagnosis and Technic, 3rd edition. By OTTO SAPHIR. 471 pp., $6.00. *Paul B. Hoeber, New York.*

Cancer Cytology of the Uterus. By J. Ernest Ayre. 407 pp., $14.50. *Grune & Stratton, New York.*

Diagnostische und Therapeutische Technik Beim Kinde. By KURT NITSCH. 168 pp., Kartoniert DM 14.70. *Georg Thieme Verlag, Stuttgart, Germany.*

Die Generalisierten Tuberkulosen. By F. Schmid. 230 pp., Kartoniert DM 24. *Georg Thieme Verlag, Stuttgart, Germany.*

Die Hämolytischen Syndrome in Kindesalter. By CONRAD GASSER. 322 pp., Ganzleinen DM 45. *Georg Thieme Verlag, Stuttgart, Germany.*

Die Neuzeitlichen Brustwant—Und Extremitäten—Ableitungen in Der Praxis. By HERBERT REINDELL and HELMUTH KLEPZIG. 179 pp., Ganzleinen DM 22.50. *Georg Thieme Verlag, Stuttgart, Germany.*

Psychosomatic Gynecology: Including Problems of Obstetrical Care. By WILLIAM S. KROGER and S. CHARLES FREED. 503 pp., $8.00 *W. B. Saunders Co., Philadelphia, Pa.*

Rosenau's Preventive Medicine and Hygiene, 7th edition. By KENNETH F. MAXCY. 1462 pp., $14.00. *Appleton-Century-Crofts, New York.*